

Rec'd PCT/PTO 14 JAN 2005

G3/03/2957



2/3
R



G803/2957



INVESTOR IN PEOPLE

42

10/52135A

PRIORITY DOCUMENT

SUBMITTED OR TRANSMITTED IN
COMPLIANCE WITH RULE 17.1(a) OR (b)

The Patent Office
Concept House
Cardiff Road
Newport
South Wales
NP10 8QQ

REC'D 21 AUG 2003

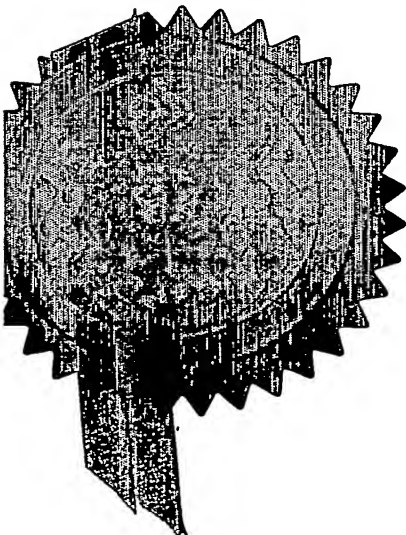
WIPO PCT

I, the undersigned, being an officer duly authorised in accordance with Section 74(1) and (4) of the Deregulation & Contracting Out Act 1994, to sign and issue certificates on behalf of the Comptroller-General, hereby certify that annexed hereto is a true copy of the documents as originally filed in connection with the patent application identified therein.

In accordance with the Patents (Companies Re-registration) Rules 1982, if a company named in this certificate and any accompanying documents has re-registered under the Companies Act 1980 with the same name as that with which it was registered immediately before re-registration save for the substitution as, or inclusion as, the last part of the name of the words "public limited company" or their equivalents in Welsh, references to the name of the company in this certificate and any accompanying documents shall be treated as references to the name with which it is so re-registered.

In accordance with the rules, the words "public limited company" may be replaced by p.l.c., plc, P.L.C. or PLC.

Re-registration under the Companies Act does not constitute a new legal entity but merely subjects the company to certain additional company law rules.



Signed

P. Mahoney

Dated

12 August 2003



17JUL02 E733792-1 C69712
P01/7700 0.00-0216525.6

Request for grant of a patent

(See the notes on the back of this form. You can also get an explanatory leaflet from the Patent Office to help you fill in this form)



The Patent Office

Cardiff Road
Newport
South Wales
NP10 8QQ

1. Your reference

138.09

2. Patent application number

(The Patent Office will fill in this part)

0216525.6

3. Full name, address and postcode of the or of each applicant (underline all surnames)

080623 5800 2
Patents ADP number (if you know it)

Incenta Limited
Incenta House
Horizon Park, Barton Road
Cambridge
CB3 7AJ

If the applicant is a corporate body, give the country/state of its incorporation

Incorporated in England

4. Title of the invention

Biologically Active Compounds

5. Name of your agent (if you have one)

"Address for service" in the United Kingdom to which all correspondence should be sent (including the postcode)

Andrew Sheard, Patent Attorney
PO Box 521
Berkhamsted
Herts.
HP4 1YP

Patents ADP number (if you know it)

08062671001

6. If you are declaring priority from one or more earlier patent applications, give the country and the date of filing of the or of each of these earlier applications and (if you know it) the or each application number

Country

Priority application number
(if you know it)

Date of filing
(day / month / year)

— no priority claimed —

7. If this application is divided or otherwise derived from an earlier UK application, give the number and the filing date of the earlier application

Number of earlier application

Date of filing
(day / month / year)

— no earlier application —

8. Is a statement of inventorship and of right to grant of a patent required in support of this request? (Answer 'Yes' if:

- a) any applicant named in part 3 is not an inventor, or
 - b) there is an inventor who is not named as an applicant, or
 - c) any named applicant is a corporate body.
- See note (d))

Yes

Patents Form 1/77

9. Enter the number of sheets for any of the following items you are filing with this form. Do not count copies of the same document

Continuation sheets of this form

None

Description

154

Claim(s)

86

Abstract

5

Drawing(s)

0

10. If you are also filing any of the following, state how many against each item.

Priority documents

Not filed

Translations of priority documents

Not filed

Statement of inventorship and right to grant of a patent (Patents Form 7/77)

Not filed

Request for preliminary examination and search (Patents Form 9/77)

Not filed

Request for substantive examination (Patents Form 10/77)

Not filed

Any other documents (please specify)

11.

I/We request the grant of a patent on the basis of this application.

Signature

A. G. Sheard

Date 16 July 2002

12. Name and daytime telephone number of person to contact in the United Kingdom

Mr A. G. Sheard, 01442 843127

Warning

After an application for a patent has been filed, the Comptroller of the Patent Office will consider whether publication or communication of the invention should be prohibited or restricted under Section 22 of the Patents Act 1977. You will be informed if it is necessary to prohibit or restrict your invention in this way. Furthermore, if you live in the United Kingdom, Section 23 of the Patents Act 1977 stops you from applying for a patent abroad without first getting written permission from the Patent Office unless an application has been filed at least 6 weeks beforehand in the United Kingdom for a patent for the same invention and either no direction prohibiting publication or communication has been given, or any such direction has been revoked.

Notes

- a) If you need help to fill in this form or you have any questions, please contact the Patent Office on 08459 500505.
- b) Write your answers in capital letters using black ink or you may type them.
- c) If there is not enough space for all the relevant details on any part of this form, please continue on a separate sheet of paper and write "see continuation sheet" in the relevant part(s). Any continuation sheet should be attached to this form.
- d) If you have answered 'Yes' Patents Form 7/77 will need to be filed.
- e) Once you have filled in the form you must remember to sign and date it.
- f) For details of the fee and ways to pay please contact the Patent Office.

BIOLOGICALLY ACTIVE COMPOUNDS

THIS INVENTION relates to compounds which are inhibitors across a broad range of cysteine proteases, to the use of these compounds, and to pharmaceutical compositions comprising them. Particular compounds of the invention are inhibitors of cathepsin K and related cysteine proteases of the CA clan. Furthermore, such compounds are useful for the *in vivo* therapeutic treatment of diseases in which participation of a cysteine protease is implicated.

Proteases form a substantial group of biological molecules which to date constitute approximately 2% of all the gene products identified following analysis of several completed genome sequencing programmes. Proteases have evolved to participate in an enormous range of biological processes, mediating their effect by cleavage of peptide amide bonds within the myriad of proteins found in nature. This hydrolytic action is performed by initially recognising, then binding to, particular three-dimensional electronic surfaces displayed by a protein, which aligns the bond for cleavage precisely within the protease catalytic site. Catalytic hydrolysis then commences through nucleophilic attack of the amide bond to be cleaved either *via* an amino acid side-chain of the protease itself, or through the action of a water molecule that is bound to and activated by the protease. Proteases in which the attacking nucleophile is the thiol side-chain of a Cys residue are known as cysteine proteases. The general classification of 'cysteine protease' contains many members found across a wide range of organisms from viruses, bacteria, protozoa, plants and fungi to mammals.

Cathepsin K and indeed many other crucial proteases belong to the papain-like CA C1 family. Cysteine proteases are classified into 'clans' based upon a similarity in the three-dimensional structure or a conserved arrangement of catalytic residues within the protease primary sequence. Additionally, 'clans' may be further classified into 'families' in which each protease shares a statistically significant relationship with other members when comparing the portions of amino acid sequence which constitute the parts responsible for the protease

activity (see Barrett, A.J *et al*, in 'Handbook of Proteolytic Enzymes', Eds. Barrett, A. J., Rawlings, N. D., and Woessner, J. F. Publ. Academic Press, 1998, for a thorough discussion).

5 To date, cysteine proteases have been classified into five clans, CA, CB, CC, CD and CE (Barrett, A. J. *et al*, 1998). A protease from the tropical papaya fruit 'papain' forms the foundation of clan CA, which currently contains over 80 distinct and complete entries in various sequence databases, with many more expected from the current genome sequencing efforts. Proteases of clan

10 CA/family C1 have been implicated in a multitude of disease processes e.g. human proteases such as cathepsin K (osteoporosis), cathepsin S (autoimmune disorders), cathepsin L (metastases) or parasitic proteases such as falcipain (malaria parasite *Plasmodium falciparum*), cruzipain (*Trypanosoma cruzi* infection). Recently a bacterial protease, staphylopain (*S. aureus* infection) has

15 also been tentatively assigned to clan CA. X-ray crystallographic structures are available for a range of the above mentioned proteases in complex with a range of inhibitors e.g. papain (PDB entries, 1pad, 1pe6, 1pip, 1pop, 4pad, 5pad, 6pad, 1ppp, 1the, 1csb, 1huc), cathepsin K (1au0, 1au2, 1au3, 1au4, 1atk, 1mem, 1bgo, 1ayw, 1ayu), cathepsin L (1cs8), cathepsin S (currently on-hold, but published

20 McGrath, M. E. *et al*, *Protein Science*, 7, 1294-1302, 1998), cruzain (a recombinant form of cruzipain see Eakin, A. E. *et al*, 268(9), 6115-6118, 1993) (1ewp, 1aim, 2aim, 1F29, 1F2A, 1F2B, 1F2C), staphylopain (1cv8). Each of the structures displays a similar overall active-site topology, as would be expected by their 'clan' and 'family' classification and such structural similarity exemplifies

25 one aspect of the difficulties involved in discovering a selective inhibitor of cathepsin K suitable for human use. However, subtle differences in terms of the depth and intricate shape of the active site groove of each CA C1 protease are evident, which may be exploited for selective inhibitor design. Additionally, many of the current substrate-based inhibitor complexes of CA C1 family proteases

30 show a series of conserved hydrogen bonds between the inhibitor and the protease backbone, which contribute significantly to inhibitor potency. Primarily a bidentate hydrogen-bond is observed between the protease Gly66 (C=O)/ inhibitor

N-H and the protease Gly66(NH)/inhibitor (C=O), where the inhibitor (C=O) and (NH) are provided by an amino acid residue NHCHRCO that constitutes the S2 sub-site binding element within the inhibitor (see Berger, A. and Schechter, I. *Philos. Trans. R. Soc. Lond. [Biol.]*, 257, 249-264, 1970 for a description of protease binding site nomenclature). A further hydrogen-bond between the protease main-chain (C=O) of asparagine or aspartic acid (158 to 163, residue number varies between proteases) and an inhibitor (N-H) is often observed, where the inhibitor (N-H) is provided by the S1 sub-site binding element within the inhibitor. Thus, the motif X-NHCHRCO-NH-Y is widely observed amongst the prior art substrate-based inhibitors of CA C1 proteases.

Cathepsin K is thought to be significant in diseases involving excessive loss of bone or cartilage. Bone consists of a protein matrix incorporating hydroxyapatite crystals. About 90% of the structural protein of the matrix is type I collagen, with the remainder comprising various non-collagenous proteins such as osteocalcin, proteoglycans, osteopontin, osteonectin, thrombospondin, fibronectin and bone sialoprotein.

Skeletal bone is not a static structure but continually undergoes a cycle of bone resorption and replacement. Bone resorption is carried out by osteoclasts, which are multinuclear cells of haematopoietic lineage. Osteoclasts adhere to the bone surface and form a tight sealing zone. The membrane on the apical surface of the osteoclasts is folded so as to create a closed extracellular compartment between the osteoclast and the bone surface, which is acidified by proton pumps in the osteoclast membrane. Proteolytic enzymes are secreted into the compartment from the osteoclast. The high acidity in the compartment causes the hydroxyapatite at the surface of the bone to be dissolved and the proteolytic enzymes break down the protein matrix causing a resorption lacuna to be formed. Following bone resorption, osteoblasts produce a new protein matrix that is subsequently mineralised.

In disease states such as osteoporosis and Paget's disease, the bone resorption and replacement cycle is disrupted leading to a net loss of bone with each cycle. This leads to weakening of the bone and therefore to increased risk of bone fracture.

5 Cathepsin K is expressed at a high level in osteoclasts and is therefore thought to be essential for bone resorption. Therefore, selective inhibition of cathepsin K is likely to be effective in the treatment of diseases involving excessive bone loss. These include osteoporosis, gingival diseases such as gingivitis and periodontitis, Paget's disease, hypercalcaemia of malignancy and metabolic bone disease.

10 In addition to osteoclasts, high levels of cathepsin K are also found in chondroclasts from the synovium of osteoarthritic patients. It therefore appears that cathepsin K inhibitors will be of use in the treatment of diseases involving matrix or cartilage degradation, in particular osteoarthritis and rheumatoid
15 arthritis.

Elevated levels of cathepsin K are also found in metastatic neoplastic cells which suggests that cathepsin K inhibitors may also be useful for treating certain neoplastic diseases.

20 In the prior art, the development of cysteine protease inhibitors for human use has recently been an area of intense activity. Considering the CA C1 family members, particular emphasis has been placed upon the development of inhibitors of human cathepsins, primarily cathepsin K (osteoporosis), cathepsin S (autoimmune
25 disorders) and cathepsin L (metastases), through the use of peptide and peptidomimetic nitriles (e.g. see WO-A-0109910, WO-A-0051998, WO-A-0119816, WO-A-9924460, WO-A-0049008, WO-A-0048992, WO-A-0049007, WO-A-0130772, WO-A-0055125, WO-A-0055126, WO-A-0119808, WO-A-0149288, WO-A-0147886), linear and cyclic peptide and peptidomimetic ketones
30 (e.g. see Veber, D. F. and Thompson, S. K., *Curr. Opin. Drug Discovery Dev.*, 3(4), 362-369, 2000, WO-A-0170232, WO-A-0178734, WO-A-0009653, WO-A-0069855, WO-A-0029408, WO-A-0134153 to WO-A-0134160, WO-A-0029408,

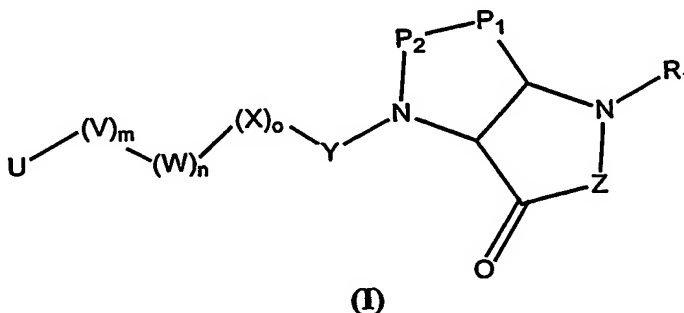
WO-A-9964399, WO-A-9805336, WO-A-9850533), ketoheterocycles (e.g. see WO-A-0055144, WO-A-0055124) and monobactams (e.g. see WO-A-0059881, WO-A-9948911, WO-A-0109169). The prior art describes potent *in vitro* inhibitors, but also highlights the many difficulties in developing a human therapeutic. For example, WO-A-9850533 and WO-A-0029408 describe compounds that may be referred to as cyclic ketones and are inhibitors of cysteine proteases with a particular reference towards papain family proteases and as a most preferred embodiment, cathepsin K. WO-A-9850533 describes compounds subsequently detailed in the literature as potent inhibitors of cathepsin K with good oral bioavailability (Witherington, J., 'Tetrahydrofurans as Selective Cathepsin K Inhibitors', RSC meeting, Burlington House, London, 1999). The compounds of WO-A-9850533 were reported to bind to cathepsin K through the formation of a reversible covalent bond between the tetrahydrofuran carbonyl and the active site catalytic cysteine residue (Witherington, J., 1999). Additionally, the same cyclic ketone compounds are described in WO-A-9953039 as part of a wide-ranging description of inhibitors of cysteine proteases associated with parasitic diseases, with particular reference to the treatment of malaria by inhibition of falcipain. However, subsequent literature describes the cyclic ketone compounds of WO-A-9850533 to be unsuitable for further development or for full pharmacokinetic evaluation due to a physiochemical property of the inhibitors, the poor chiral stability of the α -aminoketone chiral centre (Marquis, R. W. *et al*, J. Med. Chem., 44(5), 725-736, 2001). WO-A-0069855 describes compounds that may also be referred to as cyclic ketones with particular reference towards inhibition of cathepsin S. The compounds of WO-A-0069855 are considered to be an advance on compounds of WO-A-9850533 due to the presence of the β -substituent on the cyclic ketone ring system that provides chiral stability to the α -carbon of the cyclic ketone ring system. However, the compounds of WO-A-0069855 and indeed those of WO-A-9850533 describe a requirement for the presence of the potential hydrogen-bonding motif X-NHCHR₁CO-NH-Y that is widely observed amongst the prior art substrate-based inhibitors of CA C1 proteases.

-6-

Our earlier patent application (PCT/GB 02/00184) describes bicyclic compounds in which the chirality of the α -aminoketone is stabilised (for a review of energetic considerations within fused ring systems see Toromanoff, E. *Tetrahedron Report No 96*, 36, 2809-2931, 1980). These compounds do not contain the X-
 5 NHCHRCO-NH-Y motif and yet the compounds are highly potent inhibitors across a broad range of CA C1 cysteine proteases. In particular, certain of the compounds are potent and selective cruzipain inhibitors.

The present invention relates to variants of the compounds described in (PCT/GB
 10 02/00184) which are also inhibitors of a wide range of CA C1 cysteine protease. In particular, some compounds are potent and selective inhibitors of cathepsin K.

Therefore, in the present invention, there is provided a compound of general formula (I)



wherein:

$Z = CR^3R^4$, where R^3 and R^4 are independently chosen from C_{0-7} -alkyl (when $C = 0$, R^3 or R^4 is simply a hydrogen atom), C_{3-6} -cycloalkyl, Ar-
 20 C_{0-7} -alkyl (when $C = 0$, R^3 or R^4 is simply an aromatic moiety Ar),

$P_1 = CR^5R^6$, where R^5 and R^6 are independently chosen from C_{0-7} -alkyl, C_{3-6} -cycloalkyl, Ar- C_{0-7} -alkyl, O- C_{0-7} -alkyl, O- C_{3-6} -cycloalkyl, O-Ar- C_{0-7} -alkyl, S- C_{0-7} -alkyl, S- C_{3-6} -cycloalkyl, S-Ar- C_{0-7} -alkyl, NH- C_{0-7} -alkyl, NH- C_{3-6} -cycloalkyl, NH-Ar- C_{0-7} -alkyl, N(C_{0-7} -alkyl)₂, N(C_{3-6} -
 25 cycloalkyl)₂ or N(Ar- C_{0-7} -alkyl)₂;

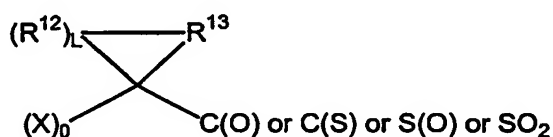
-7-

$P_2 = O, CR^7R^8$ or NR^9 , where R^7 and R^8 are independently chosen from C_{0-7} -alkyl, C_{3-6} -cycloalkyl, Ar- C_{0-7} -alkyl and R^9 is chosen from C_{0-7} -alkyl, C_{3-6} -cycloalkyl or Ar- C_{0-7} -alkyl;

5

$Y = CR^{10}R^{11}-C(O)$ or $CR^{10}R^{11}-C(S)$ or $CR^{10}R^{11}-S(O)$ or $CR^{10}R^{11}-SO_2$ where R^{10} and R^{11} are independently chosen from C_{0-7} -alkyl, C_{3-6} -cycloalkyl and Ar- C_{0-7} -alkyl, or Y represents

10



15

where L is a number from one to four and R^{12} and R^{13} are independently chosen from $CR^{14}R^{15}$ where R^{14} and R^{15} are independently chosen from C_{0-7} -alkyl, C_{3-6} -cycloalkyl, Ar- C_{0-7} -alkyl or halogen; and for each R^{12} and R^{13} either R^{14} or R^{15} (but not both R^{14} and R^{15}) may additionally be chosen from O- C_{0-7} -alkyl, O- C_{3-6} -cycloalkyl, O-Ar- C_{0-7} -alkyl, S- C_{0-7} -alkyl, S- C_{3-6} -cycloalkyl, S-Ar- C_{0-7} -alkyl, NH- C_{0-7} -alkyl, NH- C_{3-6} -cycloalkyl, NH-Ar- C_{0-7} -alkyl, N-(C_{0-7} -alkyl)₂, N-(C_{3-6} -cycloalkyl)₂, and N-(Ar- C_{0-7} -alkyl)₂;

20

$(X)_0 = CR^{16}R^{17}$, where R^{16} and R^{17} are independently chosen from C_{0-7} -alkyl, C_{3-6} -cycloalkyl and Ar- C_{0-7} -alkyl and o is a number from zero to three;

25

$(W)_n = O, S, C(O), S(O)$ or $S(O)_2$ or NR^{18} , where R^{18} is chosen from C_{0-7} -alkyl, C_{3-6} -cycloalkyl and Ar- C_{0-7} -alkyl and n is zero or one;

30

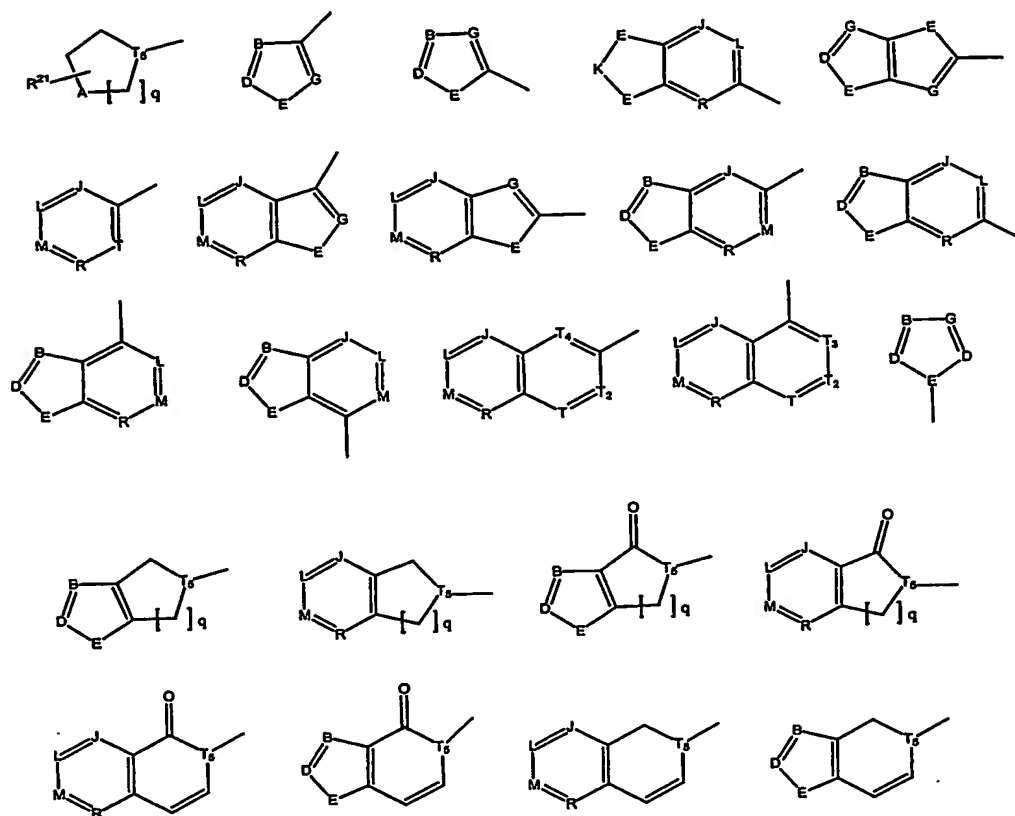
$(V)_m = C(O), C(S), S(O), S(O)_2, S(O)_2NH, OC(O), NHC(O), NHS(O), NHS(O)_2, OC(O)NH, C(O)NH$ or $CR^{19}R^{20}$, where R^{19} and R^{20} are independently chosen from C_{0-7} -alkyl, C_{3-6} -cycloalkyl, Ar- C_{0-7} -alkyl

-8-

and m is a number from zero to three, provided that when m is greater than one, $(V)_m$ contains a maximum of one carbonyl or sulphonyl group;

5

U = a stable 5- to 7-membered monocyclic or a stable 8- to 11-membered bicyclic ring which is either saturated or unsaturated and which includes zero to four heteroatoms (as detailed below):



10

wherein R^{21} is:

C_{0-7} -alkyl, C_{3-6} -cycloalkyl, Ar- C_{0-7} -alkyl, O- C_{0-7} -alkyl, O- C_{3-6} -cycloalkyl, O-Ar- C_{0-7} -alkyl, S- C_{0-7} -alkyl, S- C_{3-6} -cycloalkyl, S-Ar- C_{0-7} -alkyl, NH- C_{0-7} -alkyl, NH- C_{3-6} -cycloalkyl, NH-Ar- C_{0-7} -alkyl, $N(C_{0-7}\text{-alkyl})_2$, $N(C_{3-6}\text{-cycloalkyl})_2$

15

-9-

cycloalkyl)₂ or N(Ar-C₀₋₇-alkyl)₂; or, when part of a CHR²¹ or CR²¹ group, R²¹ may be halogen;

A is chosen from:

5 CH₂, CHR²¹, O, S, SO₂, NR²² or N-oxide (N→O), where R²¹ is as defined above; and R²² is chosen from C₀₋₇-alkyl, C₃₋₆-cycloalkyl and Ar-C₀₋₇-alkyl;

B, D and G are independently chosen from:

10 CR²¹, where R²¹ is as defined above, or N or N-oxide (N→O);

E is chosen from:

15 CH₂, CHR²¹, O, S, SO₂, NR²² or N-oxide (N→O), where R²¹ and R²² are defined as above;

K is chosen from:

CH₂, CHR²², where R²² is defined as above;

20 J, L, M, R, T, T₂, T₃ and T₄ are independently chosen from:

CR²¹ where R²¹ is as defined above, or N or N-oxide (N→O);

T₅ is chosen from:

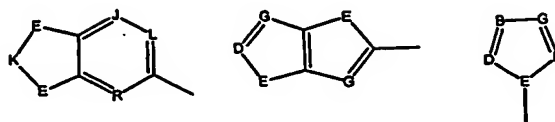
25 CH or N;

q is a number from one to three, thereby defining a 5-, 6- or 7-membered ring;

30 R¹ = R²C(O), R²OC(O), R²SO₂, where R² is chosen from C₁₋₇-alkyl, C₃₋₆-cycloalkyl or Ar-C₀₋₇-alkyl (when C = 0, R¹ is simply an aromatic moiety Ar);

-10-

provided that when Y is other than $\text{CR}^{10}\text{R}^{11}-\text{C}(\text{O})$ or when U is:



R^1 may also be C_{0-7} -alkyl, C_{3-6} -cycloalkyl or $\text{Ar}-\text{C}_{0-7}$ -alkyl.

5

The present invention includes all salts, hydrates, solvates, complexes and prodrugs of the compounds of this invention. The term "compound" is intended to include all such salts, hydrates, solvates, complexes and prodrugs, unless the context requires otherwise.

10

Appropriate pharmaceutically and veterinarily acceptable salts of the compounds of general formula (I) include salts of organic acids, especially carboxylic acids, including but not limited to acetate, trifluoroacetate, lactate, gluconate, citrate, tartrate, maleate, malate, pantothenate, adipate, alginate, aspartate, benzoate, butyrate, digluconate, cyclopentanate, glucoheptanate, glycerophosphate, oxalate, heptanoate, hexanoate, fumarate, nicotinate, palmoate, pectinate, 3-phenylpropionate, picrate, pivalate, propionate, tartrate, lactobionate, pivalate, camphorate, undecanoate and succinate, organic sulphonic acids such as methanesulphonate, ethanesulphonate, 2-hydroxyethane sulphonate, camphorsulphonate, 2-naphthalenesulphonate, benzenesulphonate, p-chlorobenzenesulphonate and p-toluenesulphonate; and inorganic acids such as hydrochloride, hydrobromide, hydroiodide, sulphate, bisulphate, hemisulphate, thiocyanate, persulphate, phosphoric and sulphonic acids. Salts which are not pharmaceutically or veterinarily acceptable may still be valuable as intermediates.

25

Prodrugs are any covalently bonded compounds which release the active parent drug according to general formula (I) *in vivo*. A prodrug may for example constitute an acetal or hemiacetal derivative of the exocyclic ketone functionality present in the hexahydropyrrolo[3,2-*b*]pyrrol-3-one, hexahydropyrrolo[3,2-

c]pyrazol-6-one or hexahydro-2-oxa-1,4-diazapentalen-6-one scaffold. If a chiral centre or another form of isomeric centre is present in a compound of the present invention, all forms of such isomer or isomers, including enantiomers and diastereoisomers, are intended to be covered herein. Compounds of the invention
5 containing a chiral centre may be used as a racemic mixture, an enantiomerically enriched mixture, or the racemic mixture may be separated using well-known techniques and an individual enantiomer may be used alone.

10 'Halogen' as applied herein is meant to include F, Cl, Br, I;

'Heteroatom' as applied herein is meant to include O, S and N;

15 'C₀₋₇-alkyl' as applied herein is meant to include stable straight and branched chain aliphatic carbon chains containing zero (*i.e.* simply hydrogen) to seven carbon atoms such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, t-butyl, pentyl, isopentyl, hexyl, heptyl and any simple isomers thereof. Additionally, where 'C₀₋₇-alkyl' contains 2 or more contiguous carbon atoms, an alkene (-CH=CH-) may be present. Additionally, any C₀₋₇-alkyl may optionally be substituted at any point by one, two or three halogen atoms (as defined above) for
20 example to give a trifluoromethyl substituent. Furthermore, C₀₋₇-alkyl may contain one or more heteroatoms (as defined above) for example to give ethers, thioethers, sulphones, sulphonamides, substituted amines, amidines, guanidines, carboxylic acids, carboxamides. If the heteroatom is located at a chain terminus then it is appropriately substituted with one or two hydrogen atoms. A heteroatom
25 or halogen is only present when C₀₋₇-alkyl contains a minimum of one carbon atom.

30 'C₃₋₆-cycloalkyl' as applied herein is meant to include any variation of 'C₀₋₇-alkyl' which additionally contains a carbocyclic ring such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl. The carbocyclic ring may optionally be substituted with one or more halogens (as defined above) or heteroatoms (as defined above) for

example to give a tetrahydrofuran, pyrrolidine, piperidine, piperazine or morpholine substituent.

5 'Ar-C₀₋₇-alkyl' as applied herein is meant to include any variation of C₀₋₇-alkyl which additionally contains an aromatic ring moiety 'Ar'. The aromatic ring moiety Ar can be a stable 5 or 6-membered monocyclic or a stable 8 to 10 membered bicyclic ring which is unsaturated, as defined previously for U in general formula (I). The aromatic ring moiety Ar may be substituted by R²¹ (as defined above for U in general formula (I)). When C = 0 in the substituent Ar-C₀₋₇-alkyl, the substituent is simply the aromatic ring moiety Ar.

15 Other expressions containing terms such as alkyl and cycloalkyl are intended to be construed according to the definitions above. For example "C₁₋₄ alkyl" is the same as C₀₋₇-alkyl except that it contains from one to four carbon atoms.

20 If different structural isomers are present, and/or one or more chiral centres are present, all isomeric forms are intended to be covered. Enantiomers are characterised by the absolute configuration of their chiral centres and described by the *R*- and *S*-sequencing rules of Cahn, Ingold and Prelog. Such conventions are well known in the art (e.g. see 'Advanced Organic Chemistry', 3rd edition, ed. March, J., John Wiley and Sons, New York, 1985). It is also intended to include compounds of general formula (I) where any hydrogen atom has been replaced by a deuterium atom.

25 Preferred compounds of general formula (I) include, but are not limited to, those in which, independently or in combination:

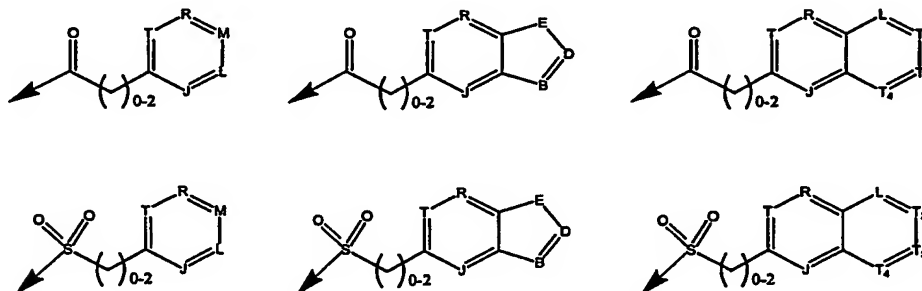
30 Z is CH₂;
P¹ is CH₂;
P² is CH₂, O or NH;
R¹ is R²C(O) or R²SO₂;

-13-

In preferred compounds of general formula (I), R^2 comprises C_{0-7} -alkyl, C_{3-6} -cycloalkyl and $Ar-C_{0-7}$ -alkyl, or more preferably C_{0-4} -alkyl, C_{3-6} -cycloalkyl and $Ar-C_{0-4}$ -alkyl, or even C_{0-2} -alkyl, C_{3-6} -cycloalkyl and $Ar-C_{0-2}$ -alkyl.

5

More preferred R^2 comprises $Ar-C_{0-2}$ -alkyl. Examples of more preferred R^2 groups include, but are not limited to:

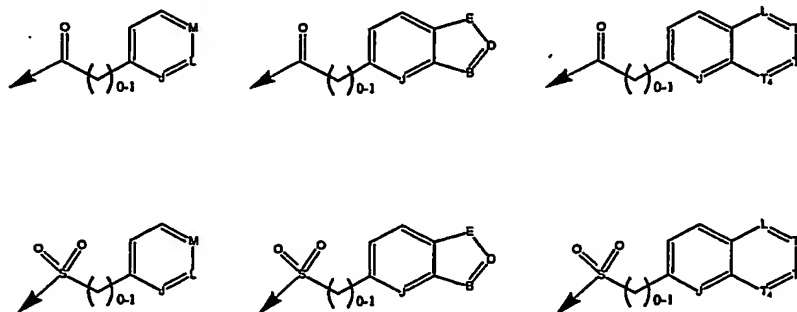


10

where J, L, M, R, T, T_2 , T_3 and T_4 are independently chosen from CR^{21} where R^{21} is as previously defined, or N or N-oxide ($N \rightarrow O$) and B, D and E are as previously defined.

Yet more preferred R^2 comprises $Ar-C_{0-1}$ -alkyl. Examples of yet more preferred R^2 groups include, but are not limited to:

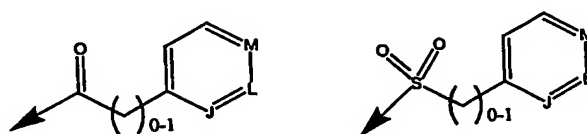
15



-14-

where J, L, M, T₂, T₃ and T₄ are independently chosen from CR²¹ where R²¹ is as previously defined, or N or N-oxide (N→O) and B, D and E are as previously defined.

- 5 Yet even more preferred R² comprises a monocyclic Ar-C₀₋₁-alkyl and include, but are not limited to:



- 10 where J, L and M are independently chosen from CR²³ where R²³ is chosen from hydrogen, methyl, methoxy, ethyl, isopropyl, *tert*-butyl, F, Cl, or J, L and M are independently chosen from N or N-oxide (N→O).

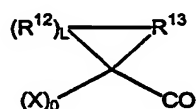
Particularly preferred R¹ groups therefore include:

- pyridine-2-sulfonyl;
 15 1-oxy-pyridine-2-sulfonyl;
 pyridine-3-sulfonyl;
 1-oxy-pyridine-3-sulfonyl;
 pyridine-2-carbonyl;
 1-oxy-pyridine-2-carbonyl;
 20 pyridine-3-carbonyl;
 1-oxy-pyridine-3-carbonyl;
 2-pyridine-3-yl-acetyl;
 pyridin-2-yl methane sulfonyl;
 pyridin-3-yl methane sulfonyl;
 25 1-oxy-pyridin-2-yl methane sulfonyl; and
 1-oxy-pyridin-3-yl methane sulfonyl.

-15-

In preferred compounds of general formula (I), Y is CHR^{11}CO where R^{11} is selected from C_{0-7} -alkyl or Ar-C_{0-7} -alkyl, for example hydrogen, a straight or branched alkyl chain, a straight or branched heteroalkyl chain, an optionally substituted arylalkyl chain or an optionally substituted arylheteroalkyl chain.

- 5 Additionally in preferred compounds of general formula (I), R^{11} is selected from C_{3-6} -cycloalkyl, for example cyclohexylmethyl or cyclopentylmethyl. Additionally, preferred compounds of general formula (I) are those in which Y comprises a group:



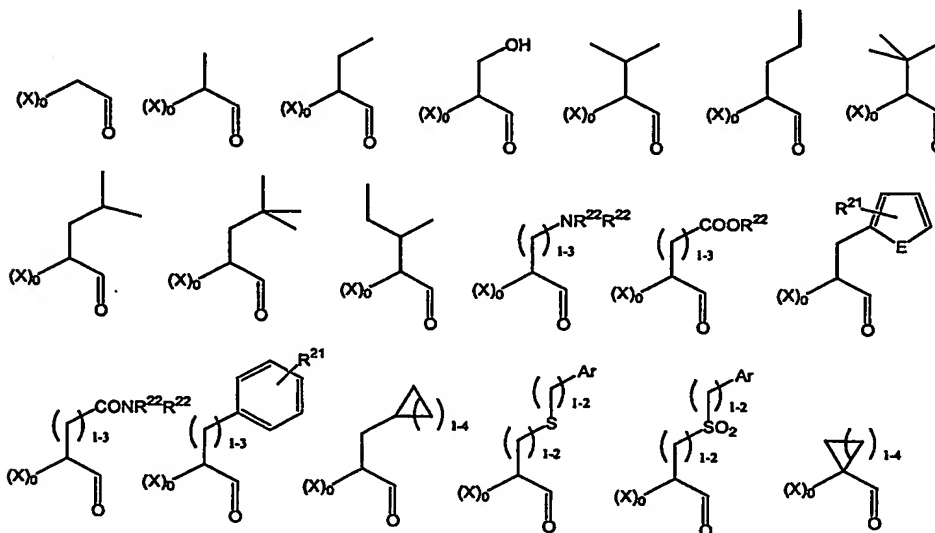
10

where R^{12} and R^{13} are each $\text{CR}^{14}\text{R}^{15}$ and each R^{14} and R^{15} is, independently, selected from C_{0-7} -alkyl or Ar-C_{0-7} -alkyl, for example hydrogen, a straight or branched alkyl chain, a straight or branched heteroalkyl chain, an optionally substituted arylalkyl chain or an optionally substituted arylheteroalkyl chain and L

15

is a number from one to four.

Examples of preferred Y substituents include, but are not limited to:



wherein E, R^{21} , R^{22} and Ar are as defined previously.

20

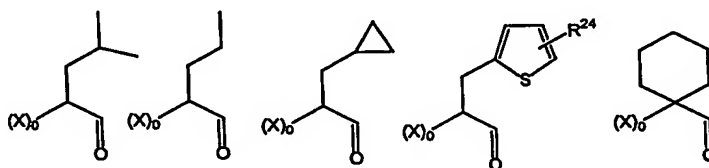
-16-

More preferred R^{11} groups include C_{1-4} -alkyl, which may be substituted with cycloalkylmethyl or R^{11} is chosen from cycloalkyl-1-carbonyl or R^{11} is chosen from Ar- C_{1-4} -alkyl, where the aryl group may be substituted with R^{21} ; where R^{21} is defined above.

5

Yet more preferred R^{11} groups comprise simple branched alkyl groups such as isobutyl or straight alkyl chains such as n-propyl. Additionally, yet more preferred R^{11} groups comprise $ArCH_2-$, where the aromatic ring is an optionally substituted monocyclic heterocycle. Furthermore, yet more preferred R^{11} groups comprise cyclopropylmethyl and cyclohexyl-1-carbonyl. Examples of yet more preferred Y

10 substituents include, but are not limited to:



wherein R^{24} is chosen from hydrogen, methyl, methoxy, ethyl, isopropyl, F, Cl.

15 Yet even more preferred R^{11} groups comprise simple branched alkyl groups such as isobutyl or n-propyl.

It is preferred that in the group $(X)_0$, each of R^{16} and R^{17} is selected from C_{0-7} -alkyl or Ar- C_{0-7} -alkyl, for example hydrogen, a straight or branched alkyl chain, a

20 straight or branched heteroalkyl chain, an optionally substituted arylalkyl chain or an optionally substituted arylheteroalkyl chain.

More preferred $(X)_0$ groups comprise R^{16} chosen from hydrogen; R^{17} chosen from hydrogen or C_{1-4} -alkyl, which may be substituted with OH, $NR^{22}R^{22}$, $COOR^{22}$, or

25 $CONR^{22}$; or Ar- C_{1-4} -alkyl, where the aryl group may be substituted with R^{21} , wherein each R^{21} and R^{22} is independently as defined previously.

-17-

Yet more preferred (X)₀ groups comprise R¹⁶ chosen from hydrogen; R¹⁷ chosen from hydrogen or simple C₁₋₄-alkyl groups such as methyl, ethyl, propyl, butyl.

5 Yet even more preferred (X)₀ groups comprise R¹⁶ and R¹⁷ as hydrogen and where o is zero or one.

It is preferred that in the group (W)_n, W is chosen from O, S, SO₂, S(O), C(O) or NR¹⁸, where R¹⁸ is chosen from C₀₋₇-alkyl; and n is 0 or 1.

10 More preferred (W)_n groups comprise O, S, SO₂, C(O) and NH where n = 0 or 1.

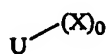
Yet more preferred (W)_n groups comprise C(O) and NH where n = 0 or 1.

15 Yet even more preferred (W)_n groups comprise NH where n = 0 or 1.

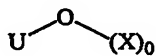
It is preferred that in the group (V)_m, V is chosen from C(O), OC(O), NHC(O), C(O)NH or CHR²⁰, where R²⁰ is C₀₋₄-alkyl and m is 0 or 1.

Preferred V and W substituent combinations include, but are not limited to:

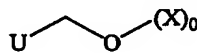
20



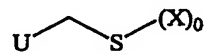
'n' = 0
'm' = 0



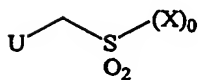
'n' = 1
'W' = O
'm' = 0



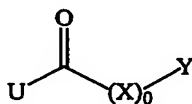
'n' = 1
'W' = O
'V' = CH₂
'm' = 1



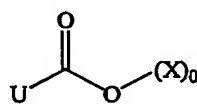
'n' = 1
'W' = S
'V' = CH₂
'm' = 1



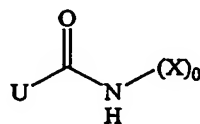
'n' = 1
'W' = SO₂
'V' = CH₂
'm' = 1



'n' = 1
'W' = C(O)
'm' = 0



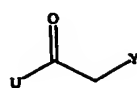
'n' = 1
'W' = O
'V' = C(O)
'm' = 1



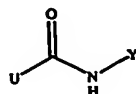
'n' = 1
'W' = NR¹⁸, R¹⁸ = 'H'
'V' = C(O)
'm' = 1

-18-

More preferred V, W and X substituent combinations include, but are not limited to:

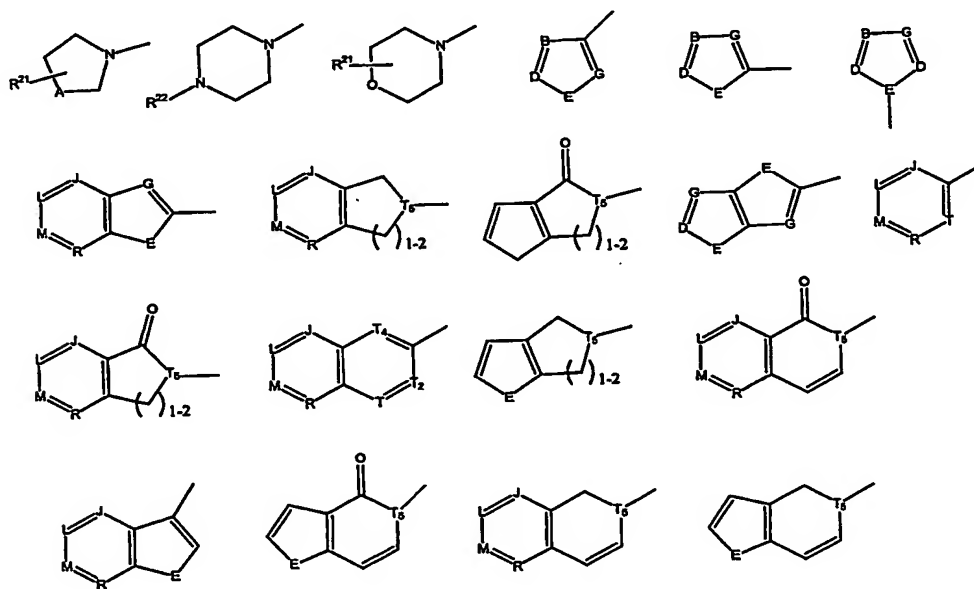


$(X)_0 = \text{'CH}_2\text{'}$
 $\text{'n'} = 1$
 $\text{'W'} = \text{C(O)}$
 $\text{'m'} = 0$



$(X)_0 = \text{'N'}$
 $\text{'n'} = 1$
 $\text{'W'} = \text{NR}^{18}$, $\text{R}^{18} = \text{'H'}$
 $\text{'V'} = \text{C(O)}$
 $\text{'m'} = 1$

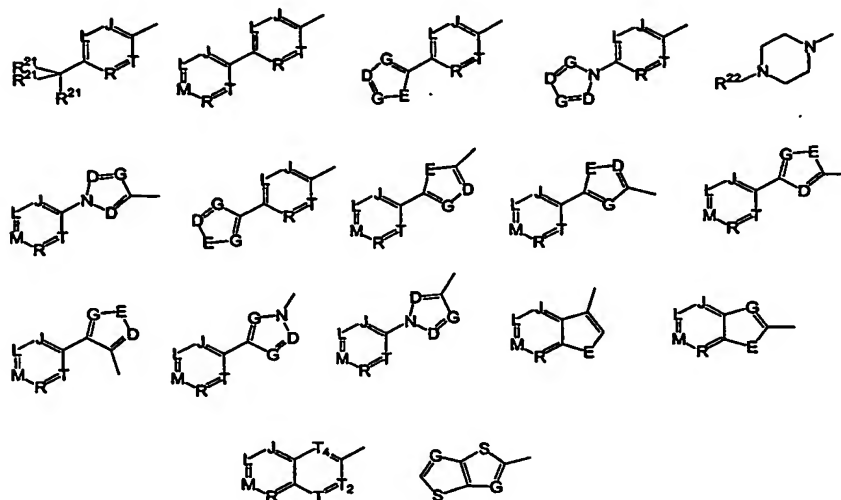
- 5 It is preferred that the group U comprises an optionally substituted 5- or 6-membered saturated or unsaturated heterocycle or Ar group or an optionally substituted saturated or unsaturated 8 to 10-membered heterocycle or Ar group. Examples of such preferred U rings include, but are not limited to the following:



- 10 wherein R^{21} , R^{22} , A, B, D, E, G, J, L, M, R, T, T_2 , T_4 and T_5 are as defined previously.

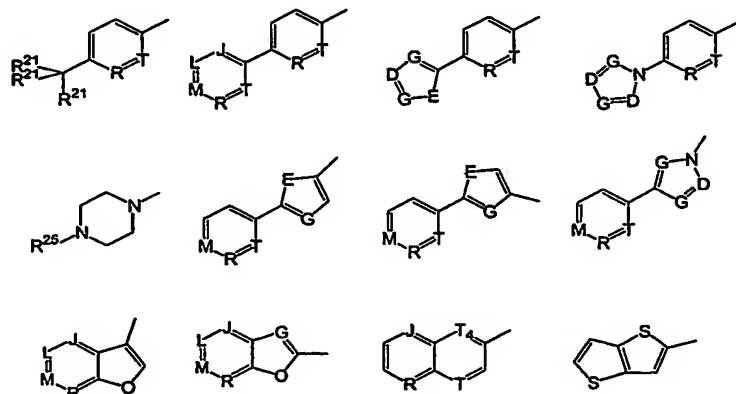
- More preferred U groups comprise of a bulky alkyl or aryl group at the para position of an aryl; a meta or para 5,6-biaryl Ar-Ar, where Ar is as previously defined; a 6,6 or 6,5 or 5,5-fused aromatic ring, where Ar is as previously defined,
- 15

or a 4-substituted piperazine. Examples of more preferred U groups include but are not limited to:



5 wherein R²¹, R²², D, E, G, J, L, M, R, T, T₂ and T₄ are as defined previously.

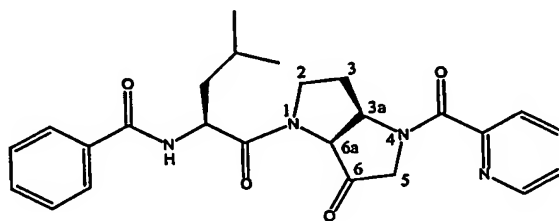
Even more preferred U groups comprise of a 6-membered aromatic ring Ar containing a bulky alkyl or aryl group at the para position; a meta or para-biaryl Ar-Ar, where Ar is as previously defined; a 6,6 or 6,5 or 5,5-fused aromatic ring, where Ar is as previously defined; or a 4-substituted piperazine where R²⁵ is chosen from C₁₋₂-alkyl or Ar-C₀₋₂-alkyl. Examples of even more preferred U groups include but are not limited to:



wherein R²¹, D, E, G, J, L, M, R, T and T₄ are as defined previously.

-20-

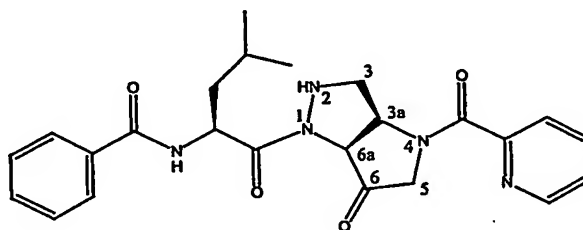
Abbreviations and symbols commonly used in the peptide and chemical arts are used herein to describe compounds of the present invention, following the general guidelines presented by the IUPAC-IUB Joint Commission on Biochemical Nomenclature as described in *Eur. J. Biochem.*, 158, 9-, 1984. Compounds of formula (I) and the intermediates and starting materials used in their preparation are named in accordance with the IUPAC rules of nomenclature in which the characteristic groups have decreasing priority for citation as the principle group. An example compound of formula (I), compound (1) in which Z is CH₂, R¹ is R²C(O), where R² is 2-pyridyl, P₁, P₂ are methylene, Y is 4-methylpentoyl, (X)₀ is zero, (W)_n is NH, (V)_m is C(O) and U is phenyl is thus named:-



(1)

(3aR,6aS) N-{3-Methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-b]pyrrole-1-carbonyl]-butyl}-benzamide;

A second example compound of formula (I), compound (2) in which Z is CH₂, R¹ is R²C(O), where R² is 2-pyridyl, P₁ is methylene, P₂ is NH, Y is 4-methylpentoyl, (X)₀ is zero, (W)_n is NH, (V)_m is C(O) and U is phenyl is thus named:-

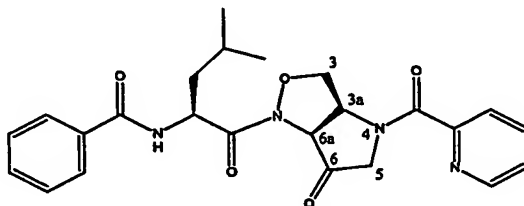


(2)

(3aR,6aS) N-{3-Methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-c]pyrazole-1-carbonyl]-butyl}-benzamide;

-21-

A third example compound of formula (I), compound (3) in which Z is CH₂, R¹ is R²C(O), where R² is 2-pyridyl, P₁ is methylene, P₂ is O, Y is 4-methylpentoyl, (X)₀ is zero, (W)_n is NH, (V)_m is C(O) and U is phenyl is thus named:-



(3)

(3a*S*, 6a*S*) N-{3-Methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-2-oxa-1,4-diazapentalene-1-carbonyl]-butyl}-benzamide.

Compounds of the invention include, but are not limited to, the following examples where all 4 stereoisomeric combinations of the bicyclic ketone are included where P₂ is CH₂, i.e. (3a*S*, 6a*S*), (3a*R*, 6a*S*), (3a*S*, 6a*R*), (3a*R*, 6a*R*) and also included are the equivalent analogues where P₂ is O and NH.

Naphthalene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

Quinoline-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

Benzo[*b*]thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

Benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

Biphenyl-4-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

4-*tert*-Butyl-N-{3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

4-Dimethylamino-N-{3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

- 7-Methoxy-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 {3-Methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-carbamic acid benzyl ester;
- 5-Methoxy-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 Thieno[3,2-*b*]thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 3-Methyl-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Quinoxaline-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 20 Benzo[1,3]dioxole-5-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Quinoline-6-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 25 Furan-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 Thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- N-{3-Methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethyl-benzamide;
- 35 Furan-3-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thiophene-3-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 N-{3-Methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-phenoxy-benzamide;
- 45 N-{3-Methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-(4-methyl-piperazin-1-yl)-benzamide;
- 4-Methyl-N-{3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

- 4-Methoxy-N-{3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 5 4-Isopropyl-N-{3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- N-{3-Methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-vinyl-benzamide;
- 10 4-Imidazol-1-yl-N-{3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- N-{3-Methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-thiophen-2-yl-benzamide;
- 15 N-{3-Methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-oxazol-5-yl-benzamide;
- 20 5-Phenyl-thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- N-{3-Methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethoxy-benzamide;
- 25 5-Pyridin-2-yl-thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 4-Difluoromethoxy-N-{3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 30 N-{3-Methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-morpholin-4-yl-benzamide;
- 35 Naphthalene-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Quinoline-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 Benzo[*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 Biphenyl-4-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

- 4-*tert*-Butyl-N-{1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 5 4-Dimethylamino-N-{1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 7-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-carbamic acid benzyl ester;
- 15 5-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 20 3-Methyl-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Quinoxaline-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 25 Benzo[1,3]dioxole-5-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 Quinoline-6-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Furan-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 35 Thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- N-{1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethyl-benzamide;
- 40 Furan-3-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 Thiophene-3-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- N-{1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-phenoxy-benzamide;

- N-{1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-(4-methyl-piperazin-1-yl)-benzamide;
- 5 4-Methyl-N-{1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Methoxy-N-{1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 10 4-Isopropyl-N-{1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 15 N-{1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-vinyl-benzamide;
- 4-Imidazol-1-yl-N-{1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 20 N-{1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-thiophen-2-yl-benzamide;
- N-{1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-oxazol-5-yl-benzamide;
- 25 5-Phenyl-thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 N-{1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethoxy-benzamide;
- 5-Pyridin-2-yl-thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 35 4-Difluoromethoxy-N-{1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- N-{1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-morpholin-4-yl-benzamide;
- 40 Naphthalene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 Quinoline-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzo[*b*]thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

- Benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 Biphenyl-4-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 4-*tert*-Butyl-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 10 4-Dimethylamino-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 15 7-Methoxy-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- {3-Methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-carbamic acid benzyl ester;
- 20 5-Methoxy-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thieno[3,2-*b*]thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 25 3-Methyl-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 Quinoxaline-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzo[1,3]dioxole-5-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 35 Quinoline-6-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Furan-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 Thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethyl-benzamide;
- Furan-3-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

Thiophene-3-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

5 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-phenoxy-benzamide;

N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-(4-methyl-piperazin-1-yl)-benzamide;

10

4-Methyl-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

15 4-Methoxy-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

4-Isopropyl-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

20 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-vinyl-benzamide;

4-Imidazol-1-yl-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

25

N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-thiophen-2-yl-benzamide;

30 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-oxazol-5-yl-benzamide;

5-Phenyl-thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

35 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethoxy-benzamide;

5-Pyridin-2-yl-thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

40

4-Difluoromethoxy-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

45 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-morpholin-4-yl-benzamide;

Naphthalene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

- Quinoline-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 Benzo[*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 Biphenyl-4-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 4-*tert*-Butyl-N-{1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Dimethylamino-N-{1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 20 7-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-carbamic acid benzyl ester;
- 25 5-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 3-Methyl-benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 35 Quinoxaline-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzo[1,3]dioxole-5-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 Quinoline-6-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 Furan-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

- N-{1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethyl-benzamide;
- 5 Furan-3-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thiophene-3-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 N-{1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-phenoxy-benzamide;
- 15 N-{1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-(4-methyl-piperazin-1-yl)-benzamide;
- 4-Methyl-N-{1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 20 4-Methoxy-N-{1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Isopropyl-N-{1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 25 N-{1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-vinyl-benzamide;
- 4-Imidazol-1-yl-N-{1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 30 N-{1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-thiophen-2-yl-benzamide;
- 35 N-{1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-oxazol-5-yl-benzamide;
- 5-Phenyl-thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 N-{1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethoxy-benzamide;
- 5-Pyridin-2-yl-thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 4-Difluoromethoxy-N-{1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

- N-{1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-morpholin-4-yl-benzamide;
- 5 Naphthalene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Quinoline-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 Benzo[*b*]thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 Benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Biphenyl-4-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 20 4-*tert*-Butyl-N-{3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Dimethylamino-N-{3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 25 7-Methoxy-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 {3-Methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-carbamic acid benzyl ester;
- 5-Methoxy-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 35 Thieno[3,2-*b*]thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 3-Methyl-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 Quinoxaline-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 Benzo[1,3]dioxole-5-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Quinoline-6-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

- Furan-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 Thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- N-{3-Methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethyl-benzamide;
- 10 Furan-3-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 Thiophene-3-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- N-{3-Methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-phenoxy-benzamide;
- 20 N-{3-Methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-(4-methyl-piperazin-1-yl)-benzamide;
- 4-Methyl-N-{3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 25 4-Methoxy-N-{3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 30 4-Isopropyl-N-{3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- N-{3-Methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-vinyl-benzamide;
- 35 4-Imidazol-1-yl-N-{3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- N-{3-Methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-thiophen-2-yl-benzamide;
- 40 N-{3-Methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-oxazol-5-yl-benzamide;
- 45 5-Phenyl-thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- N-{3-Methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethoxy-benzamide;

- 5-Pyridin-2-yl-thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 4-Difluoromethoxy-N-{3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- N-{3-Methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-morpholin-4-yl-benzamide;
- 10 Naphthalene-2-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 Quinoline-2-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzo[*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 20 Benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Biphenyl-4-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 25 4-*tert*-Butyl-N-{1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 30 4-Dimethylamino-N-{1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 7-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 35 {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-carbamic acid benzyl ester;
- 5-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 3-Methyl-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 Quinoxaline-2-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

Benzo[1,3]dioxole-5-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

5 Quinoline-6-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

Furan-2-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

10 Thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

15 N-{1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethyl-benzamide;

Furan-3-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

20 Thiophene-3-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

N-{1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-phenoxy-benzamide;

25 N-{1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-(4-methyl-piperazin-1-yl)-benzamide;

30 4-Methyl-N-{1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

4-Methoxy-N-{1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

35 4-Isopropyl-N-{1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

N-{1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-vinyl-benzamide;

40 4-Imidazol-1-yl-N-{1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

45 N-{1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-thiophen-2-yl-benzamide;

N-{1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-oxazol-5-yl-benzamide;

- 5-Phenyl-thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 N-{1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethoxy-benzamide;
- 5-Pyridin-2-yl-thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 4-Difluoromethoxy-N-{1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 15 N-{1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-morpholin-4-yl-benzamide;
- Naphthalene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 20 Quinoline-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzo[*b*]thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 25 Benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 Biphenyl-4-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 4-*tert*-Butyl-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 35 4-Dimethylamino-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 7-Methoxy-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 {3-Methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-carbamic acid benzyl ester;
- 45 5-Methoxy-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thieno[3,2-*b*]thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

- 3-Methyl-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 Quinoxaline-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzo[1,3]dioxole-5-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 Quinoline-6-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 Furan-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 20 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethyl-benzamide;
- Furan-3-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 25 Thiophene-3-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-phenoxy-benzamide;
- N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-(4-methyl-piperazin-1-yl)-benzamide;
- 35 4-Methyl-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Methoxy-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 40 4-Isopropyl-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 45 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-vinyl-benzamide;
- 4-Imidazol-1-yl-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

- N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-thiophen-2-yl-benzamide;
- 5 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-oxazol-5-yl-benzamide;
- 5-Phenyl-thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethoxy-benzamide;
- 5-Pyridin-2-yl-thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 4-Difluoromethoxy-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 20 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-morpholin-4-yl-benzamide;
- Naphthalene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 25 Quinoline-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzo[*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 Benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 35 Biphenyl-4-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 4-*tert*-Butyl-N-{1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 40 4-Dimethylamino-N-{1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 7-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-carbamic acid benzyl ester;

- 5-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 3-Methyl-benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 Quinoxaline-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 Benzo[1,3]dioxole-5-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Quinoline-6-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 20 Furan-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 25 N-{1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethyl-benzamide;
- Furan-3-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 Thiophene-3-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 35 N-{1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-phenoxy-benzamide;
- N-{1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-(4-methyl-piperazin-1-yl)-benzamide;
- 40 4-Methyl-N-{1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Methoxy-N-{1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 45 4-Isopropyl-N-{1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

- N-{1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-vinyl-benzamide;
- 5 4-Imidazol-1-yl-N-{1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- N-{1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-thiophen-2-yl-benzamide;
- 10 N-{1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-oxazol-5-yl-benzamide;
- 15 5-Phenyl-thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- N-{1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethoxy-benzamide;
- 20 5-Pyridin-2-yl-thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 4-Difluoromethoxy-N-{1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 25 N-{1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-morpholin-4-yl-benzamide;
- 30 Naphthalene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Quinoline-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 35 Benzo[*b*]thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzo[*f*]furan-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 Biphenyl-4-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 4-*tert*-Butyl-N-{3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Dimethylamino-N-{3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

- 7-Methoxy-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 {3-Methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-carbamic acid benzyl ester;
- 5-Methoxy-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 Thieno[3,2-*b*]thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 3-Methyl-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Quinoxaline-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 20 Benzo[1,3]dioxole-5-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Quinoline-6-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 25 Furan-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 Thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- N-{3-Methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethyl-benzamide;
- 35 Furan-3-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thiophene-3-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 N-{3-Methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-phenoxy-benzamide;
- N-{3-Methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-(4-methyl-piperazin-1-yl)-benzamide;
- 45 4-Methyl-N-{3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

- 4-Methoxy-N-{3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 5 4-Isopropyl-N-{3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- N-{3-Methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-vinyl-benzamide;
- 10 4-Imidazol-1-yl-N-{3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 15 N-{3-Methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-thiophen-2-yl-benzamide;
- N-{3-Methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-oxazol-5-yl-benzamide;
- 20 5-Phenyl-thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- N-{3-Methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethoxy-benzamide;
- 25 5-Pyridin-2-yl-thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 4-Difluoromethoxy-N-{3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- N-{3-Methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-morpholin-4-yl-benzamide;
- 35 Naphthalene-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Quinoline-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 Benzo[*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 Benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Biphenyl-4-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

- 4-*tert*-Butyl-N-{1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 5 4-Dimethylamino-N-{1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 7-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-carbamic acid benzyl ester;
- 15 5-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 20 3-Methyl-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Quinoxaline-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 25 Benzo[1,3]dioxole-5-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 Quinoline-6-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Furan-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 35 Thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- N-{1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethyl-benzamide;
- 40 Furan-3-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 Thiophene-3-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- N-{1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-phenoxy-benzamide;

- N-{1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-(4-methyl-piperazin-1-yl)-benzamide;
- 5 4-Methyl-N-{1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Methoxy-N-{1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 10 4-Isopropyl-N-{1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 15 N-{1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-vinyl-benzamide;
- 4-Imidazol-1-yl-N-{1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 20 N-{1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-thiophen-2-yl-benzamide;
- N-{1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-oxazol-5-yl-benzamide;
- 25 5-Phenyl-thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 N-{1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethoxy-benzamide;
- 5-Pyridin-2-yl-thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 35 4-Difluoromethoxy-N-{1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- N-{1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-morpholin-4-yl-benzamide;
- 40 Naphthalene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 Quinoline-2-carboxylic acid {3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzo[*b*]thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

- Benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 Biphenyl-4-carboxylic acid {3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 4-*tert*-Butyl-N-{3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 10 4-Dimethylamino-N-{3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 15 7-Methoxy-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- {3-Methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-carbamic acid benzyl ester;
- 20 5-Methoxy-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thieno[3,2-*b*]thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 25 3-Methyl-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 Quinoxaline-2-carboxylic acid {3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzo[1,3]dioxole-5-carboxylic acid {3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 35 Quinoline-6-carboxylic acid {3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Furan-2-carboxylic acid {3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 Thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- N-{3-Methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethyl-benzamide;
- 45 Furan-3-carboxylic acid {3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

Thiophene-3-carboxylic acid {3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

5 N-{3-Methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-phenoxy-benzamide;

N-{3-Methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-(4-methyl-piperazin-1-yl)-benzamide;

10 4-Methyl-N-{3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

15 4-Methoxy-N-{3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

4-Isopropyl-N-{3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

20 N-{3-Methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-vinyl-benzamide;

4-Imidazol-1-yl-N-{3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

25 N-{3-Methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-thiophen-2-yl-benzamide;

30 N-{3-Methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-oxazol-5-yl-benzamide;

5-Phenyl-thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

35 N-{3-Methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethoxy-benzamide;

5-Pyridin-2-yl-thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

40 4-Difluoromethoxy-N-{3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

45 N-{3-Methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-morpholin-4-yl-benzamide;

Naphthalene-2-carboxylic acid {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

- Quinoline-2-carboxylic acid {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 Benzo[*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 Benzofuran-2-carboxylic acid {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 Biphenyl-4-carboxylic acid {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 4-*tert*-Butyl-N-{1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 20 4-Dimethylamino-N-{1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 25 7-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-carbamic acid benzyl ester;
- 30 5-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 35 3-Methyl-benzofuran-2-carboxylic acid {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 Quinoxaline-2-carboxylic acid {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzo[1,3]dioxole-5-carboxylic acid {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 Furan-2-carboxylic acid {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thiophene-2-carboxylic acid {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

- N-{1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethyl-benzamide;
- 5 Furan-3-carboxylic acid {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thiophene-3-carboxylic acid {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 N-{1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-phenoxy-benzamide;
- 15 N-{1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-(4-methyl-piperazin-1-yl)-benzamide;
- 4-Methyl-N-{1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 20 4-Methoxy-N-{1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Isopropyl-N-{1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 25 N-{1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-vinyl-benzamide;
- 30 4-Imidazol-1-yl-N-{1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- N-{1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-thiophen-2-yl-benzamide;
- 35 N-{1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-oxazol-5-yl-benzamide;
- 5-Phenyl-thiophene-2-carboxylic acid {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 N-{1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethoxy-benzamide;
- 45 5-Pyridin-2-yl-thiophene-2-carboxylic acid {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 4-Difluoromethoxy-N-{1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

N-{1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-morpholin-4-yl-benzamide;

5 Naphthalene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

Quinoline-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

10 Benzo[*b*]thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

15 Benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

Biphenyl-4-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

20 4-*tert*-Butyl-N-{3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

4-Dimethylamino-N-{3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

25 7-Methoxy-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

30 {3-Methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-carbamic acid benzyl ester;

5-Methoxy-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

35 Thieno[3,2-*b*]thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

3-Methyl-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

40 Quinoxaline-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

45 Benzo[1,3]dioxole-5-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

Quinoline-6-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

- Furan-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 Thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- N-{3-Methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethyl-benzamide;
- 10 Furan-3-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 Thiophene-3-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- N-{3-Methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-phenoxy-benzamide;
- 20 N-{3-Methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-(4-methyl-piperazin-1-yl)-benzamide;
- 4-Methyl-N-{3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 25 4-Methoxy-N-{3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 30 4-Isopropyl-N-{3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- N-{3-Methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-vinyl-benzamide;
- 35 4-Imidazol-1-yl-N-{3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- N-{3-Methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-thiophen-2-yl-benzamide;
- 40 N-{3-Methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-oxazol-5-yl-benzamide;
- 45 5-Phenyl-thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- N-{3-Methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethoxy-benzamide;

- 5-Pyridin-2-yl-thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 4-Difluoromethoxy-N-{3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- N-{3-Methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-morpholin-4-yl-benzamide;
- 10 Naphthalene-2-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 Quinoline-2-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzo[*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 20 Benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Biphenyl-4-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 25 4-*tert*-Butyl-N-{1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 30 4-Dimethylamino-N-{1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 7-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 35 {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-carbamic acid benzyl ester;
- 5-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 3-Methyl-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 Quinoxaline-2-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

- Benzo[1,3]dioxole-5-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 Quinoline-6-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Furan-2-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 Thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 N-{1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethyl-benzamide;
- Furan-3-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 20 Thiophene-3-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- N-{1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-phenoxy-benzamide;
- 25 N-{1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-(4-methyl-piperazin-1-yl)-benzamide;
- 30 4-Methyl-N-{1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Methoxy-N-{1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 35 4-Isopropyl-N-{1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- N-{1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-vinyl-benzamide;
- 40 4-Imidazol-1-yl-N-{1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 45 N-{1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-thiophen-2-yl-benzamide;
- N-{1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-oxazol-5-yl-benzamide;

- 5-Phenyl-thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 N-{1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethoxy-benzamide;
- 5-Pyridin-2-yl-thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 4-Difluoromethoxy-N-{1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 15 N-{1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-morpholin-4-yl-benzamide;
- Naphthalene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 20 Quinoline-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzo[*b*]thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 25 Benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Biphenyl-4-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 4-*tert*-Butyl-N-{3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 35 4-Dimethylamino-N-{3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 7-Methoxy-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 {3-Methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-carbamic acid benzyl ester;
- 45 5-Methoxy-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thieno[3,2-*b*]thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

- 3-Methyl-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 Quinoxaline-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzo[1,3]dioxole-5-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 Quinoline-6-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 Furan-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 20 N-{3-Methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethyl-benzamide;
- Furan-3-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 25 Thiophene-3-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 N-{3-Methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-phenoxy-benzamide;
- N-{3-Methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-(4-methyl-piperazin-1-yl)-benzamide;
- 35 4-Methyl-N-{3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Methoxy-N-{3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 40 4-Isopropyl-N-{3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 45 N-{3-Methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-vinyl-benzamide;
- 4-Imidazol-1-yl-N-{3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

N-{3-Methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-thiophen-2-yl-benzamide;

5 N-{3-Methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-oxazol-5-yl-benzamide;

10 5-Phenyl-thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

N-{3-Methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethoxy-benzamide;

15 5-Pyridin-2-yl-thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

4-Difluoromethoxy-N-{3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

20 N-{3-Methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-morpholin-4-yl-benzamide;

25 Naphthalene-2-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

Quinoline-2-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

30 Benzo[*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

Benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

35 Biphenyl-4-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

40 4-*tert*-Butyl-N-{1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

4-Dimethylamino-N-{1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

45 7-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

{1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-carbamic acid benzyl ester;

- 5-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 3-Methyl-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 Quinoxaline-2-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 Benzo[1,3]dioxole-5-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Quinoline-6-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 20 Furan-2-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 25 N-{1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethyl-benzamide;
- 30 Furan-3-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thiophene-3-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 35 N-{1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-phenoxy-benzamide;
- N-{1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-(4-methyl-piperazin-1-yl)-benzamide;
- 40 4-Methyl-N-{1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 45 4-Methoxy-N-{1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Isopropyl-N-{1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

- N-{1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-vinyl-benzamide;
- 5 4-Imidazol-1-yl-N-{1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- N-{1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-thiophen-2-yl-benzamide;
- 10 N-{1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-oxazol-5-yl-benzamide;
- 15 5-Phenyl-thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- N-{1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethoxy-benzamide;
- 20 5-Pyridin-2-yl-thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 4-Difluoromethoxy-N-{1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 25 N-{1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-morpholin-4-yl-benzamide;
- 30 Naphthalene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Quinoline-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 35 Benzo[*b*]thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzo[*f*]furan-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 Biphenyl-4-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 4-*tert*-Butyl-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Dimethylamino-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

- 7-Methoxy-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 {3-Methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-carbamic acid benzyl ester;
- 5-Methoxy-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 Thieno[3,2-*b*]thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 3-Methyl-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Quinoxaline-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 20 Benzo[1,3]dioxole-5-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Quinoline-6-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 25 Furan-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 Thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethyl-benzamide;
- 35 Furan-3-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thiophene-3-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-phenoxy-benzamide;
- 45 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-(4-methyl-piperazin-1-yl)-benzamide;
- 4-Methyl-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

- 4-Methoxy-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 5 4-Isopropyl-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 10 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-vinyl-benzamide;
- 15 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-thiophen-2-yl-benzamide;
- 20 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-oxazol-5-yl-benzamide;
- 25 5-Phenyl-thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethoxy-benzamide;
- 35 5-Pyridin-2-yl-thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 4-Difluoromethoxy-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 45 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-morpholin-4-yl-benzamide;
- Naphthalene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Quinoline-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzo[*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

- Biphenyl-4-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 4-*tert*-Butyl-N-{1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Dimethylamino-N-{1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 10 7-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-carbamic acid benzyl ester;
- 15 5-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 20 Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 3-Methyl-benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 25 Quinoxaline-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzo[1,3]dioxole-5-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 Quinoline-6-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 35 Furan-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 N-{1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethyl-benzamide;
- Furan-3-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 Thiophene-3-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

- N-{1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-phenoxy-benzamide;
- 5 N-{1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-(4-methyl-piperazin-1-yl)-benzamide;
- 4-Methyl-N-{1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 10 4-Methoxy-N-{1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Isopropyl-N-{1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 15 N-{1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-vinyl-benzamide;
- 4-Imidazol-1-yl-N-{1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 20 N-{1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-thiophen-2-yl-benzamide;
- 25 N-{1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-oxazol-5-yl-benzamide;
- 5-Phenyl-thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 N-{1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethoxy-benzamide;
- 5-Pyridin-2-yl-thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 35 4-Difluoromethoxy-N-{1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 40 N-{1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-morpholin-4-yl-benzamide;
- Naphthalene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 Quinoline-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

- Benzo[b]thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 Benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Biphenyl-4-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 4-*tert*-Butyl-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Dimethylamino-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 15 7-Methoxy-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- {3-Methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-carbamic acid benzyl ester;
- 20 5-Methoxy-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 25 Thieno[3,2-*b*]thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 3-Methyl-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 Quinoxaline-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzo[1,3]dioxole-5-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 35 Quinoline-6-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 Furan-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethyl-benzamide;

- Furan-3-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 Thiophene-3-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-phenoxy-benzamide;
- 10 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-(4-methyl-piperazin-1-yl)-benzamide;
- 4-Methyl-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 15 4-Methoxy-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Isopropyl-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 20 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-vinyl-benzamide;
- 25 4-Imidazol-1-yl-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-thiophen-2-yl-benzamide;
- 30 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-oxazol-5-yl-benzamide;
- 5-Phenyl-thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 35 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethoxy-benzamide;
- 40 5-Pyridin-2-yl-thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 4-Difluoromethoxy-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 45 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-morpholin-4-yl-benzamide;

- Naphthalene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 Quinoline-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzo[*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 Benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 Biphenyl-4-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 4-*tert*-Butyl-N-{1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 20 4-Dimethylamino-N-{1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 7-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 25 {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-carbamic acid benzyl ester;
- 5-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 35 3-Methyl-benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Quinoxaline-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 Benzo[1,3]dioxole-5-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 Quinoline-6-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Furan-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

Thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

- 5 N-{1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethyl-benzamide;

Furan-3-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

10

Thiophene-3-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

15

N-{1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-phenoxy-benzamide;

N-{1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-(4-methyl-piperazin-1-yl)-benzamide;

20

4-Methyl-N-{1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

4-Methoxy-N-{1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

25

4-Isopropyl-N-{1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

30

N-{1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-vinyl-benzamide;

4-Imidazol-1-yl-N-{1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

35

N-{1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-thiophen-2-yl-benzamide;

N-{1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-oxazol-5-yl-benzamide;

40

5-Phenyl-thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

45

N-{1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethoxy-benzamide;

5-Pyridin-2-yl-thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

- 4-Difluoromethoxy-N-{1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 5 N-{1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-morpholin-4-yl-benzamide;
- 4-*tert*-Butyl-N-{1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-benzamide;
- 10 5-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 15 Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 3-Methyl-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 20 N-{1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-4-phenoxy-benzamide;
- N-{1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-4-thiophen-2-yl-benzamide;
- 25 4-*tert*-Butyl-N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 30 5-Methoxy-benzofuran-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 35 3-Methyl-benzofuran-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-4-phenoxy-benzamide;
- 40 N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-4-thiophen-2-yl-benzamide;
- 45 4-*tert*-Butyl-N-{2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-benzamide;

- 5-Methoxy-benzofuran-2-carboxylic acid {2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 5 Thieno[3,2-*b*]thiophene-2-carboxylic acid {2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 10 3-Methyl-benzofuran-2-carboxylic acid {2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- N-{2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-4-phenoxy-benzamide;
- 15 N-{2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-4-thiophen-2-yl-benzamide;
- 4-*tert*-Butyl-N-{1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-benzamide;
- 20 5-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 25 Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 3-Methyl-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 30 N-{1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-4-phenoxy-benzamide;
- N-{1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-4-thiophen-2-yl-benzamide;
- 35 4-*tert*-Butyl-N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 40 5-Methoxy-benzofuran-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 45 3-Methyl-benzofuran-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;

- N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-4-phenoxy-benzamide;
- 5 N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-4-thiophen-2-yl-benzamide;
- 4-*tert*-Butyl-N-{2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-benzamide;
- 10 5-Methoxy-benzofuran-2-carboxylic acid {2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 15 Thieno[3,2-*b*]thiophene-2-carboxylic acid {2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 3-Methyl-benzofuran-2-carboxylic acid {2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 20 N-{2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-4-phenoxy-benzamide;
- 25 N-{2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-4-thiophen-2-yl-benzamide;
- 4-*tert*-Butyl-N-{1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-benzamide;
- 30 5-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 35 3-Methyl-benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 40 N-{1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-4-phenoxy-benzamide;
- N-{1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-4-thiophen-2-yl-benzamide;
- 45 4-*tert*-Butyl-N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;

- 5-Methoxy-benzofuran-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 5 Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 10 3-Methyl-benzofuran-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-4-phenoxy-benzamide;
- 15 N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-4-thiophen-2-yl-benzamide;
- 4-*tert*-Butyl-N-{2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-benzamide;
- 20 5-Methoxy-benzofuran-2-carboxylic acid {2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 25 Thieno[3,2-*b*]thiophene-2-carboxylic acid {2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 30 3-Methyl-benzofuran-2-carboxylic acid {2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- N-{2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-4-phenoxy-benzamide;
- 35 N-{2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-4-thiophen-2-yl-benzamide;
- 40 4-*tert*-Butyl-N-{1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-benzamide;
- 5-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 45 Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;

- 3-Methyl-benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 5 N-{1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-4-phenoxy-benzamide;
- N-{1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-4-thiophen-2-yl-benzamide;
- 10 4-*tert*-Butyl-N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 5-Methoxy-benzofuran-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 15 Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 20 3-Methyl-benzofuran-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-4-phenoxy-benzamide;
- 25 N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-4-thiophen-2-yl-benzamide;
- 30 4-*tert*-Butyl-N-{2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-benzamide;
- 5-Methoxy-benzofuran-2-carboxylic acid {2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 35 Thieno[3,2-*b*]thiophene-2-carboxylic acid {2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 40 3-Methyl-benzofuran-2-carboxylic acid {2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 45 N-{2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-4-phenoxy-benzamide;

- N-{2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-4-thiophen-2-yl-benzamide;
- 5 4-*tert*-Butyl-N-{1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-benzamide;
- 5-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 10 Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 3-Methyl-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 15 N-{1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-4-phenoxy-benzamide;
- 20 N-{1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-4-thiophen-2-yl-benzamide;
- 4-*tert*-Butyl-N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 25 5-Methoxy-benzofuran-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 30 3-Methyl-benzofuran-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 35 N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-4-phenoxy-benzamide;
- N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-4-thiophen-2-yl-benzamide;
- 40 4-*tert*-Butyl-N-{2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-benzamide;
- 5-Methoxy-benzofuran-2-carboxylic acid {2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 45

- Thieno[3,2-*b*]thiophene-2-carboxylic acid {2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 5 3-Methyl-benzofuran-2-carboxylic acid {2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 10 N-{2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-4-phenoxy-benzamide;
- 15 4-*tert*-Butyl-N-{1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-benzamide;
- 5-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 20 Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 25 3-Methyl-benzofuran-2-carboxylic acid {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- N-{1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-4-phenoxy-benzamide;
- 30 N-{1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-4-thiophen-2-yl-benzamide;
- 4-*tert*-Butyl-N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 35 5-Methoxy-benzofuran-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 40 Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 3-Methyl-benzofuran-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 45 N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-4-phenoxy-benzamide;
- N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-4-thiophen-2-yl-benzamide;

- 4-*tert*-Butyl-N-{2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-benzamide;
- 5 5-Methoxy-benzofuran-2-carboxylic acid {2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 10 Thieno[3,2-*b*]thiophene-2-carboxylic acid {2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 15 3-Methyl-benzofuran-2-carboxylic acid {2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- N-{2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-4-phenoxy-benzamide;
- 20 N-{2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-4-thiophen-2-yl-benzamide;
- 25 4-*tert*-Butyl-N-{1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-benzamide;
- 5-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 30 Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 35 3-Methyl-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 40 N-{1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-4-phenoxy-benzamide;
- N-{1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-4-thiophen-2-yl-benzamide;
- 45 4-*tert*-Butyl-N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;

-72-

- 5-Methoxy-benzofuran-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 5 Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 10 3-Methyl-benzofuran-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 15 N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-4-phenoxy-benzamide;
- 20 4-*tert*-Butyl-N-{2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-benzamide;
- 25 5-Methoxy-benzofuran-2-carboxylic acid {2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 30 Thieno[3,2-*b*]thiophene-2-carboxylic acid {2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 35 3-Methyl-benzofuran-2-carboxylic acid {2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- N-{2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-4-phenoxy-benzamide;
- N-{2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-4-thiophen-2-yl-benzamide;
- 40 4-*tert*-Butyl-N-{1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-benzamide;
- 45 5-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;

- Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 5 3-Methyl-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 10 N-{1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-4-phenoxy-benzamide;
- N-{1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-4-thiophen-2-yl-benzamide;
- 15 4-*tert*-Butyl-N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 20 5-Methoxy-benzofuran-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 25 Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 3-Methyl-benzofuran-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 30 N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-4-phenoxy-benzamide;
- N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-4-thiophen-2-yl-benzamide;
- 35 4-*tert*-Butyl-N-{2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-benzamide;
- 40 5-Methoxy-benzofuran-2-carboxylic acid {2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 45 Thieno[3,2-*b*]thiophene-2-carboxylic acid {2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;

- 3-Methyl-benzofuran-2-carboxylic acid {2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 5 N-{2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-4-phenoxy-benzamide;
- N-{2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-4-thiophen-2-yl-benzamide;
- 10 4-*tert*-Butyl-N-{1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-benzamide;
- 15 5-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 20 Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 25 3-Methyl-benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- N-{1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-4-phenoxy-benzamide;
- 30 N-{1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-4-thiophen-2-yl-benzamide;
- 4-*tert*-Butyl-N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 35 5-Methoxy-benzofuran-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 40 Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 45 3-Methyl-benzofuran-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-4-phenoxy-benzamide;

- N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-4-thiophen-2-yl-benzamide;
- 5 4-*tert*-Butyl-N-{2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-benzamide;
- 10 5-Methoxy-benzofuran-2-carboxylic acid {2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 15 Thieno[3,2-*b*]thiophene-2-carboxylic acid {2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 20 3-Methyl-benzofuran-2-carboxylic acid {2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 25 N-{2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-4-phenoxy-benzamide;
- N-{2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-4-thiophen-2-yl-benzamide;
- 30 4-*tert*-Butyl-N-{1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-benzamide;
- 35 5-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 40 Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 45 3-Methyl-benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- N-{1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-4-phenoxy-benzamide;
- N-{1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-4-thiophen-2-yl-benzamide;

- 4-*tert*-Butyl-N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 5 5-Methoxy-benzofuran-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 10 Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 15 3-Methyl-benzofuran-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 20 N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-4-phenoxy-benzamide;
- N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-4-thiophen-2-yl-benzamide;
- 25 4-*tert*-Butyl-N-{2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-benzamide;
- 5-Methoxy-benzofuran-2-carboxylic acid {2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 30 Thieno[3,2-*b*]thiophene-2-carboxylic acid {2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 35 3-Methyl-benzofuran-2-carboxylic acid {2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 40 N-{2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-4-thiophen-2-yl-benzamide;
- 45 2-Isobutyl-4-morpholin-4-yl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 2-Isobutyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-piperazin-1-yl-butane-1,4-dione;

- 2-Isobutyl-4-(4-methyl-piperazin-1-yl)-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 5 2-Isobutyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(4-phenyl-piperazin-1-yl)-butane-1,4-dione;
- 2-Isobutyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(3,4,4a,8a-tetrahydro-1H-isoquinolin-2-yl)-butane-1,4-dione;
- 10 2-Isobutyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(1,3,3a,7a-tetrahydro-isoindol-2-yl)-butane-1,4-dione;
- 15 4-(4-Benzyl-piperazin-1-yl)-2-isobutyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 2-Isobutyl-4-morpholin-4-yl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 20 2-Isobutyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-piperazin-1-yl-butane-1,4-dione;
- 2-Isobutyl-4-(4-methyl-piperazin-1-yl)-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 25 2-Isobutyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(4-phenyl-piperazin-1-yl)-butane-1,4-dione;
- 30 2-Isobutyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(3,4,4a,8a-tetrahydro-1H-isoquinolin-2-yl)-butane-1,4-dione;
- 2-Isobutyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(1,3,3a,7a-tetrahydro-isoindol-2-yl)-butane-1,4-dione;
- 35 4-(4-Benzyl-piperazin-1-yl)-2-isobutyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 2-Isobutyl-4-morpholin-4-yl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 40 2-Isobutyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-piperazin-1-yl-butane-1,4-dione;
- 45 2-Isobutyl-4-(4-methyl-piperazin-1-yl)-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 2-Isobutyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(4-phenyl-piperazin-1-yl)-butane-1,4-dione;

- 2-Isobutyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-
b]pyrrol-1-yl]-4-(3,4,4a,8a-tetrahydro-1H-isoquinolin-2-yl)-butane-1,4-dione;
- 5 2-Isobutyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-
b]pyrrol-1-yl]-4-(1,3,3a,7a-tetrahydro-isoindol-2-yl)-butane-1,4-dione;
- 4-(4-Benzyl-piperazin-1-yl)-2-isobutyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-
hexahydro-pyrrolo[3,2-b]pyrrol-1-yl]-butane-1,4-dione;
- 10 2-Isobutyl-4-morpholin-4-yl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-
pyrrolo[3,2-b]pyrrol-1-yl]-butane-1,4-dione;
- 15 2-Isobutyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-
b]pyrrol-1-yl]-4-piperazin-1-yl-butane-1,4-dione;
- 2-Isobutyl-4-(4-methyl-piperazin-1-yl)-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-
hexahydro-pyrrolo[3,2-b]pyrrol-1-yl]-butane-1,4-dione;
- 20 2-Isobutyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-
b]pyrrol-1-yl]-4-(4-phenyl-piperazin-1-yl)-butane-1,4-dione;
- 2-Isobutyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-
b]pyrrol-1-yl]-4-(3,4,4a,8a-tetrahydro-1H-isoquinolin-2-yl)-butane-1,4-dione;
- 25 2-Isobutyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-
b]pyrrol-1-yl]-4-(1,3,3a,7a-tetrahydro-isoindol-2-yl)-butane-1,4-dione;
- 4-(4-Benzyl-piperazin-1-yl)-2-isobutyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-
hexahydro-pyrrolo[3,2-b]pyrrol-1-yl]-butane-1,4-dione;
- 30 2-Isobutyl-4-morpholin-4-yl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-
pyrrolo[3,2-b]pyrrol-1-yl]-butane-1,4-dione;
- 35 2-Isobutyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-b]pyrrol-1-
yl]-4-piperazin-1-yl-butane-1,4-dione;
- 2-Isobutyl-4-(4-methyl-piperazin-1-yl)-1-[6-oxo-4-(pyridine-2-carbonyl)-
hexahydro-pyrrolo[3,2-b]pyrrol-1-yl]-butane-1,4-dione;
- 40 2-Isobutyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-b]pyrrol-1-
yl]-4-(4-phenyl-piperazin-1-yl)-butane-1,4-dione;
- 2-Isobutyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-b]pyrrol-1-
yl]-4-(3,4,4a,8a-tetrahydro-1H-isoquinolin-2-yl)-butane-1,4-dione;
- 45 2-Isobutyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-b]pyrrol-1-
yl]-4-(1,3,3a,7a-tetrahydro-isoindol-2-yl)-butane-1,4-dione;

- 4-(4-Benzyl-piperazin-1-yl)-2-isobutyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 5 2-Isobutyl-4-morpholin-4-yl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 2-Isobutyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-piperazin-1-yl-butane-1,4-dione;
- 10 2-Isobutyl-4-(4-methyl-piperazin-1-yl)-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 15 2-Isobutyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(4-phenyl-piperazin-1-yl)-butane-1,4-dione;
- 2-Isobutyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(3,4,4a,8a-tetrahydro-1H-isoquinolin-2-yl)-butane-1,4-dione;
- 20 2-Isobutyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(1,3,3a,7a-tetrahydro-isoindol-2-yl)-butane-1,4-dione;
- 4-(4-Benzyl-piperazin-1-yl)-2-isobutyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 25 2-Isobutyl-4-morpholin-4-yl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 30 2-Isobutyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-piperazin-1-yl-butane-1,4-dione;
- 2-Isobutyl-4-(4-methyl-piperazin-1-yl)-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 35 2-Isobutyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(4-phenyl-piperazin-1-yl)-butane-1,4-dione;
- 2-Isobutyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(3,4,4a,8a-tetrahydro-1H-isoquinolin-2-yl)-butane-1,4-dione;
- 40 2-Isobutyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(1,3,3a,7a-tetrahydro-isoindol-2-yl)-butane-1,4-dione;
- 45 4-(4-Benzyl-piperazin-1-yl)-2-isobutyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 2-Isobutyl-4-morpholin-4-yl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;

- 2-Isobutyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-
b]pyrrol-1-yl]-4-piperazin-1-yl-butane-1,4-dione;
- 5 2-Isobutyl-4-(4-methyl-piperazin-1-yl)-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-
hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 2-Isobutyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-
b]pyrrol-1-yl]-4-(4-phenyl-piperazin-1-yl)-butane-1,4-dione;
- 10 2-Isobutyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-
b]pyrrol-1-yl]-4-(3,4,4a,8a-tetrahydro-1H-isoquinolin-2-yl)-butane-1,4-dione;
- 15 2-Isobutyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-
b]pyrrol-1-yl]-4-(1,3,3a,7a-tetrahydro-isoindol-2-yl)-butane-1,4-dione;
- 4-(4-Benzyl-piperazin-1-yl)-2-isobutyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-
hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 20 2-Isobutyl-4-morpholin-4-yl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-
hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 2-Isobutyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-
pyrrolo[3,2-*b*]pyrrol-1-yl]-4-piperazin-1-yl-butane-1,4-dione;
- 25 2-Isobutyl-4-(4-methyl-piperazin-1-yl)-1-[6-oxo-4-(1-oxy-pyridin-2-
ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 2-Isobutyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-
pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(4-phenyl-piperazin-1-yl)-butane-1,4-dione;
- 30 2-Isobutyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-
pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(3,4,4a,8a-tetrahydro-1H-isoquinolin-2-yl)-butane-
1,4-dione;
- 35 2-Isobutyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-
pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(1,3,3a,7a-tetrahydro-isoindol-2-yl)-butane-1,4-
dione;
- 40 4-(4-Benzyl-piperazin-1-yl)-2-isobutyl-1-[6-oxo-4-(1-oxy-pyridin-2-
ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 2-Isobutyl-4-morpholin-4-yl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-
hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 45 2-Isobutyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-
pyrrolo[3,2-*b*]pyrrol-1-yl]-4-piperazin-1-yl-butane-1,4-dione;

- 2-Isobutyl-4-(4-methyl-piperazin-1-yl)-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 5 2-Isobutyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(4-phenyl-piperazin-1-yl)-butane-1,4-dione;
- 10 2-Isobutyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(3,4,4a,8a-tetrahydro-1H-isoquinolin-2-yl)-butane-1,4-dione;
- 15 4-(4-Benzyl-piperazin-1-yl)-2-isobutyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 20 4-(2-Biphenyl-3-yl-4-methyl-pentanoyl)-1-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 25 4-(2-Biphenyl-3-yl-4-methyl-pentanoyl)-1-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 30 4-(2-Biphenyl-3-yl-4-methyl-pentanoyl)-1-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 35 4-(2-Biphenyl-3-yl-4-methyl-pentanoyl)-1-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 40 4-(2-Biphenyl-3-yl-4-methyl-pentanoyl)-1-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 45 4-(2-Biphenyl-3-yl-4-methyl-pentanoyl)-1-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 4-(2-Biphenyl-3-yl-4-methyl-pentanoyl)-1-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 4-(2-Biphenyl-3-yl-4-methyl-pentanoyl)-1-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 4-(2-Biphenyl-3-yl-4-methyl-pentanoyl)-1-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 4-(2-Biphenyl-3-yl-4-methyl-pentanoyl)-1-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;

- 4-[4-Methyl-2-(3-pyridin-2-yl-phenyl)-pentanoyl]-1-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 5 4-[4-Methyl-2-(3-pyridin-2-yl-phenyl)-pentanoyl]-1-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 4-[4-Methyl-2-(3-pyridin-2-yl-phenyl)-pentanoyl]-1-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 10 4-[4-Methyl-2-(3-pyridin-2-yl-phenyl)-pentanoyl]-1-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 4-[4-Methyl-2-(3-pyridin-2-yl-phenyl)-pentanoyl]-1-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 15 4-[4-Methyl-2-(3-pyridin-2-yl-phenyl)-pentanoyl]-1-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 4-[4-Methyl-2-(3-pyridin-2-yl-phenyl)-pentanoyl]-1-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 20 4-[4-Methyl-2-(3-pyridin-2-yl-phenyl)-pentanoyl]-1-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 4-[4-Methyl-2-(3-pyridin-2-yl-phenyl)-pentanoyl]-1-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 25 4-[4-Methyl-2-(3-pyridin-2-yl-phenyl)-pentanoyl]-1-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 30 4-[4-Methyl-2-(3-pyridin-3-yl-phenyl)-pentanoyl]-1-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 4-[4-Methyl-2-(3-pyridin-3-yl-phenyl)-pentanoyl]-1-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 35 4-[4-Methyl-2-(3-pyridin-3-yl-phenyl)-pentanoyl]-1-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 4-[4-Methyl-2-(3-pyridin-3-yl-phenyl)-pentanoyl]-1-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 40 4-[4-Methyl-2-(3-pyridin-3-yl-phenyl)-pentanoyl]-1-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 45 4-[4-Methyl-2-(3-pyridin-3-yl-phenyl)-pentanoyl]-1-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;

-83-

4-[4-Methyl-2-(3-pyridin-3-yl-phenyl)-pentanoyl]-1-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;

5 4-[4-Methyl-2-(3-pyridin-3-yl-phenyl)-pentanoyl]-1-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;

4-[4-Methyl-2-(3-pyridin-3-yl-phenyl)-pentanoyl]-1-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;

10 4-[4-Methyl-2-(3-pyridin-3-yl-phenyl)-pentanoyl]-1-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;

15 4-[4-Methyl-2-(3-pyridin-4-yl-phenyl)-pentanoyl]-1-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;

4-[4-Methyl-2-(3-pyridin-4-yl-phenyl)-pentanoyl]-1-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;

20 4-[4-Methyl-2-(3-pyridin-4-yl-phenyl)-pentanoyl]-1-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;

4-[4-Methyl-2-(3-pyridin-4-yl-phenyl)-pentanoyl]-1-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;

25 4-[4-Methyl-2-(3-pyridin-4-yl-phenyl)-pentanoyl]-1-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;

30 4-[4-Methyl-2-(3-pyridin-4-yl-phenyl)-pentanoyl]-1-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;

4-[4-Methyl-2-(3-pyridin-4-yl-phenyl)-pentanoyl]-1-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;

35 4-[4-Methyl-2-(3-pyridin-4-yl-phenyl)-pentanoyl]-1-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;

4-[4-Methyl-2-(3-pyridin-4-yl-phenyl)-pentanoyl]-1-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;

40 4-[4-Methyl-2-(3-pyridin-4-yl-phenyl)-pentanoyl]-1-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one.

45 Other compounds of the invention include, but are not limited to, the following examples where all 4 stereoisomeric combinations of the bicyclic ketone are

included where P₂ is CH₂, i.e. (3a*S*, 6a*S*), (3a*R*, 6a*S*), (3a*S*, 6a*R*), (3a*R*, 6a*R*) and also included are the equivalent analogues where P₂ is O and NH.

- 5 Furan-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thiophene-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 Benzo[*b*]thiophene-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Furan-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 15 Thiophene-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 20 Benzo[*b*]thiophene-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Naphthalene-1-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 25 Quinoline-8-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 4-*tert*-Butyl-N-{1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 30 4-*tert*-Butyl-N-{1-(4-fluoro-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 35 4-*tert*-Butyl-N-{1-(4-methoxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 4-*tert*-Butyl-N-{1-(3-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 40 Biphenyl-4-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Biphenyl-4-carboxylic acid {1-(4-fluoro-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 45 Biphenyl-4-carboxylic acid {1-(4-methoxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;

- Biphenyl-4-carboxylic acid {1-(3-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 5 Furan-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thiophene-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 Benzo[*b*]thiophene-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 Furan-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Thiophene-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 20 Benzo[*b*]thiophene-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Naphthalene-1-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 25 Quinoline-8-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 30 4-*tert*-Butyl-N-{1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 4-*tert*-Butyl-N-{1-(4-fluoro-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 35 4-*tert*-Butyl-N-{1-(4-methoxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 4-*tert*-Butyl-N-{1-(3-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 40 Biphenyl-4-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 45 Biphenyl-4-carboxylic acid {1-(4-fluoro-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Biphenyl-4-carboxylic acid {1-(4-methoxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;

- Biphenyl-4-carboxylic acid {1-(3-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 5 Furan-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thiophene-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 Benzo[*b*]thiophene-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 Furan-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Thiophene-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 20 Benzo[*b*]thiophene-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Naphthalene-1-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 25 Quinoline-8-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 30 4-*tert*-Butyl-N-{1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 4-*tert*-Butyl-N-{1-(4-fluoro-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 35 4-*tert*-Butyl-N-{1-(4-methoxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 4-*tert*-Butyl-N-{1-(3-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 40 Biphenyl-4-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 45 Biphenyl-4-carboxylic acid {1-(4-fluoro-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Biphenyl-4-carboxylic acid {1-(4-methoxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;

Biphenyl-4-carboxylic acid {1-(3-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;

- 5 Furan-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

Thiophene-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

10

Benzo[*b*]thiophene-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

15

Furan-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;

Thiophene-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;

20

Benzo[*b*]thiophene-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;

Naphthalene-1-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;

25

Quinoline-8-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;

30

4-*tert*-Butyl-N-{1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;

4-*tert*-Butyl-N-{1-(4-fluoro-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;

35

4-*tert*-Butyl-N-{1-(4-methoxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;

4-*tert*-Butyl-N-{1-(3-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;

40

Biphenyl-4-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;

Biphenyl-4-carboxylic acid {1-(4-fluoro-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;

45

Biphenyl-4-carboxylic acid {1-(4-methoxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;

- Biphenyl-4-carboxylic acid {1-(3-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 5 Furan-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thiophene-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 Benzo[*b*]thiophene-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Furan-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 15 Thiophene-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 20 Benzo[*b*]thiophene-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Naphthalene-1-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 25 Quinoline-8-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 4-*tert*-Butyl-N-{1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 30 4-*tert*-Butyl-N-{1-(4-fluoro-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 35 4-*tert*-Butyl-N-{1-(4-methoxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 4-*tert*-Butyl-N-{1-(3-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 40 Biphenyl-4-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 45 Biphenyl-4-carboxylic acid {1-(4-fluoro-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Biphenyl-4-carboxylic acid {1-(4-methoxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;

- Biphenyl-4-carboxylic acid {1-(3-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 5 Furan-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thiophene-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 Benzo[*b*]thiophene-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 Furan-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Thiophene-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 20 Benzo[*b*]thiophene-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Naphthalene-1-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 25 Quinoline-8-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 30 4-*tert*-Butyl-N-{1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 4-*tert*-Butyl-N-{1-(4-fluoro-benzyl)-2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 35 4-*tert*-Butyl-N-{1-(4-methoxy-benzyl)-2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 4-*tert*-Butyl-N-{1-(3-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 40 Biphenyl-4-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 45 Biphenyl-4-carboxylic acid {1-(4-fluoro-benzyl)-2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Biphenyl-4-carboxylic acid {1-(4-methoxy-benzyl)-2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;

- Biphenyl-4-carboxylic acid {1-(3-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 5 Furan-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thiophene-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 Benzo[*b*]thiophene-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 Furan-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Thiophene-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 20 Benzo[*b*]thiophene-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 25 Naphthalene-1-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Quinoline-8-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 30 4-*tert*-Butyl-N-{1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 35 4-*tert*-Butyl-N-{1-(4-fluoro-benzyl)-2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 40 4-*tert*-Butyl-N-{1-(4-methoxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- Biphenyl-4-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 45 Biphenyl-4-carboxylic acid {1-(4-fluoro-benzyl)-2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;

- Biphenyl-4-carboxylic acid {1-(4-methoxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 5 Biphenyl-4-carboxylic acid {1-(3-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Furan-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 Thiophene-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzo[*b*]thiophene-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 Furan-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 20 Thiophene-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Benzo[*b*]thiophene-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 25 Naphthalene-1-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 30 Quinoline-8-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 4-*tert*-Butyl-N-{1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 35 4-*tert*-Butyl-N-{1-(4-fluoro-benzyl)-2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 40 4-*tert*-Butyl-N-{1-(4-methoxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 45 4-*tert*-Butyl-N-{1-(3-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- Biphenyl-4-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Biphenyl-4-carboxylic acid {1-(4-fluoro-benzyl)-2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;

- Biphenyl-4-carboxylic acid {1-(4-methoxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 5 Biphenyl-4-carboxylic acid {1-(3-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Furan-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 Thiophene-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 Benzo[*b*]thiophene-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Furan-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 20 Thiophene-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 25 Benzo[*b*]thiophene-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Naphthalene-1-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 30 Quinoline-8-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 4-*tert*-Butyl-N-{1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 35 4-*tert*-Butyl-N-{1-(4-fluoro-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 40 4-*tert*-Butyl-N-{1-(4-methoxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 4-*tert*-Butyl-N-{1-(3-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 45 Biphenyl-4-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;

- Biphenyl-4-carboxylic acid {1-(4-fluoro-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 5 Biphenyl-4-carboxylic acid {1-(4-methoxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Biphenyl-4-carboxylic acid {1-(3-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 10 Furan-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 Thiophene-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzo[*b*]thiophene-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 20 Furan-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Thiophene-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 25 Benzo[*b*]thiophene-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 30 Naphthalene-1-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Quinoline-8-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 35 4-*tert*-Butyl-N-{1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 40 4-*tert*-Butyl-N-{1-(4-fluoro-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 4-*tert*-Butyl-N-{1-(4-methoxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 45 4-*tert*-Butyl-N-{1-(3-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- Biphenyl-4-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;

Biphenyl-4-carboxylic acid {1-(4-fluoro-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;

5 Biphenyl-4-carboxylic acid {1-(4-methoxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;

10 Biphenyl-4-carboxylic acid {1-(3-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
2-Cyclohexylmethyl-4-morpholin-4-yl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;

15 2-Cyclohexylmethyl-4-morpholin-4-yl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;

2-Cyclohexylmethyl-4-morpholin-4-yl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;

20 2-Cyclohexylmethyl-4-morpholin-4-yl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;

2-Cyclohexylmethyl-4-morpholin-4-yl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;

25 2-Cyclohexylmethyl-4-morpholin-4-yl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;

30 2-Cyclohexylmethyl-4-morpholin-4-yl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;

2-Cyclohexylmethyl-4-morpholin-4-yl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;

35 2-Cyclohexylmethyl-4-morpholin-4-yl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;

2-Cyclohexylmethyl-4-morpholin-4-yl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;

40 2-(2,2-Dimethyl-propyl)-4-morpholin-4-yl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;

45 2-(2,2-Dimethyl-propyl)-4-morpholin-4-yl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;

2-(2,2-Dimethyl-propyl)-4-morpholin-4-yl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;

2-(2,2-Dimethyl-propyl)-4-morpholin-4-yl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;

5 2-(2,2-Dimethyl-propyl)-4-morpholin-4-yl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;

10 2-(2,2-Dimethyl-propyl)-4-morpholin-4-yl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;

2-(2,2-Dimethyl-propyl)-4-morpholin-4-yl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;

15 2-(2,2-Dimethyl-propyl)-4-morpholin-4-yl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;

2-(2,2-Dimethyl-propyl)-4-morpholin-4-yl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;

20 2-(2,2-Dimethyl-propyl)-4-morpholin-4-yl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione.

25 To those skilled in the practices of organic chemistry, compounds of general formula (I) may be readily synthesised by a number of chemical strategies, performed either in solution or on the solid phase (see Atherton, E. and Sheppard, R. C. In *'Solid Phase Peptide Synthesis: A Practical Approach'*, Oxford University Press, Oxford, U.K. 1989, for a general review of solid phase synthesis principles). The solid phase strategy is attractive in being able to generate many
30 thousands of analogues, typically on a 5-100mg scale, through established parallel synthesis methodologies (e.g. see (a) Bastos, M.; Maeji, N. J.; Abeles, R. H. *Proc. Natl. Acad. Sci. USA*, 92, 6738-6742, 1995).

Therefore, one strategy for the synthesis of compounds of general formula (I)
35 comprises:-

(a) Preparation of an appropriately functionalised and protected bicyclic ketone building block in solution.

(b) Attachment of the building block (a) to the solid phase through a linker that is stable to the conditions of synthesis, but readily labile to cleavage at the end of a synthesis (see James, I. W., *Tetrahedron*, 55(Report N° 489), 4855-4946, 1999, for examples of the 'linker' function as applied to solid phase synthesis).

(c) Solid phase organic chemistry (see Brown, R. D. *J. Chem. Soc., Perkin Trans.1*, 19, 3293-3320, 1998), to construct the remainder of the molecule.

(d) Compound cleavage from the solid phase into solution.

(e) Cleavage work-up and compound analysis.

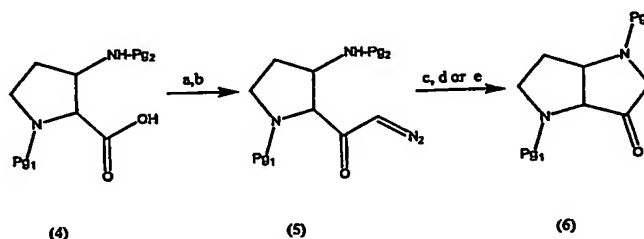
10

The first stage in a synthesis of compounds of general formula (I) is the preparation in solution of a functionalised and protected building block. Typical schemes towards the hexahydropyrrolo[3,2-*b*]pyrrol-3-one (6) are detailed in Schemes 1-3, a hexahydropyrrolo[3,2-*c*]pyrazol-6-one (21) in Scheme 4 and a hexahydro-2-oxa-1,4-diazapentalen-6-one (26) in Scheme 5. The synthetic descriptions detailed in Schemes 6-18 could equally be applied using each of the scaffolds of general formula (I).

15

'Pg₁' and 'Pg₂' denotes suitable amine protecting groups such as the 9-fluorenyl methoxycarbonyl (Fmoc, see Atherton, E. and Sheppard, R. C. In '*Solid Phase Peptide Synthesis: A Practical Approach*', Oxford University Press, Oxford, U.K. 1989), *tert*-butoxycarbonyl (Boc), benzyloxycarbonyl (Cbz) or allyloxycarbonyl (Alloc) for example.

20



25

Scheme 1. (a) ^tBuOCOCl, NMM, DCM, -15°C, under argon. (b) Diazomethane in diethyl ether, -15°C, 30mins, then RT overnight. (c) LiCl (10eq) in 80%aq acetic acid RT overnight. (d) HBr / acetic acid followed by re-addition of Pg₂ (if 'Pg₂' is Boc). (e) Rh(II)(OAc)₄, DCM, reflux.

In the illustrated case, condensation with diazomethane provides $Z = \text{CH}_2$ in general formula (I). Synthesis may commence from a suitably protected β -aminoproline (4) which are described in the literature e.g. Gomez-Vidal, J. A. and Silverman, R. B. *Org. Lett.*, 3(16), 2481-2484, 2001.

Activation of the suitably protected β -aminoproline (4) via isobutyl chloroformate mixed anhydride, followed by condensation with diazomethane, yields the diazomethylketone intermediate (5). Treatment of diazomethylketone intermediate (5) with lithium chloride in aqueous acetic acid provides the protected hexahydropyrrolo[3,2-*b*]pyrrol-3-one (6). Alternatively, when Pg_2 is Boc, treatment with HBr in acetic acid provides an intermediate bicycle with the secondary amine. HBr salt. This intermediate may be acylated with a variety of reagents e.g. activated carboxylic acids, sulphonyl chlorides, urethane chloroformates to provide many variations of (6) where the nitrogen substituent is a suitable protecting group ' Pg_2 ' or $\text{R}^2\text{C}(\text{O})$, R^2SO_2 , etc. Alternatively, treatment of diazomethylketone intermediate (5) with rhodium (II) tetraacetate in dichloromethane provides the hexahydropyrrolo[3,2-*b*]pyrrol-3-one (6) (e.g. see Lall, M. S. *et al*, *J. Org. Chem.*, 67, 1536-1547, 2002. and refs cited therein).

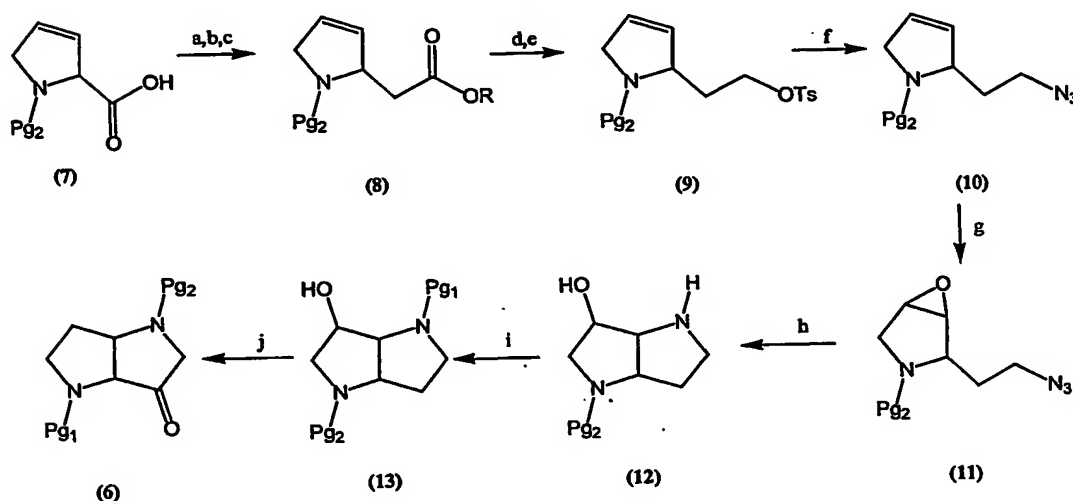
Introduction of simple 'Z' substituents may be achieved by condensation of activated (5) with alternatives to diazomethane such as diazoethane ($Z = \text{CHCH}_3$, $\text{R}^3 = \text{H}$, $\text{R}^4 = \text{CH}_3$), or 1-phenyloxydiazoethane ($Z = \text{CHCH}_2\text{OPh}$, $\text{R}^3 = \text{H}$, $\text{R}^4 = \text{CH}_2\text{OPh}$).

An alternative route towards a suitably protected building block is detailed in Scheme 2. Using an Arndt-Eistert synthesis, a suitably protected 3,4-dehydroproline (7) may be homologated by methylene insertion between the α -carbon and carboxylic acid following standard literature methods (e.g. see Meier and Zeller, *Angew. Chem. Intl. Ed. Engl.*, 14, 32-43, 1975 for a review). Conversion of (7) into the α -diazomethylketone proceeds via isobutyl chloroformate mixed anhydride, followed by condensation with diazomethane.

-98-

Wolff rearrangement, e.g. with silver oxide in methanol provides the protected homologated analogue (8), e.g. 2-Methoxycarbonylmethyl-2,5-dihydro-pyrrole-1-carboxylic acid tert-butyl ester.

5



Scheme 2. (a) $t\text{BuOCOC}\text{Cl}$, NMM, DCM, -15°C , under argon. (b) Diazomethane in diethyl ether, -15°C , 30mins, then RT overnight. (c) Arndt-Eistert, e.g. Silver oxide in methanol ($R = \text{CH}_3$). (d) DIBAL reduction. (e) Tosylchloride, pyridine. (f) Sodium azide, DCM / DMF (g) *m*-chloroperbenzoic acid, DCM. (h) Azide reduction to amine, e.g. Pd-C / H_2 in ethanol. (i) Secondary amine protection, ' Pg_1 ' e.g. 1.05 eq Fmoc-Cl, 2.1eq Na_2CO_3 , dioxan, water. (j) Dess-Martin periodane, DCM.

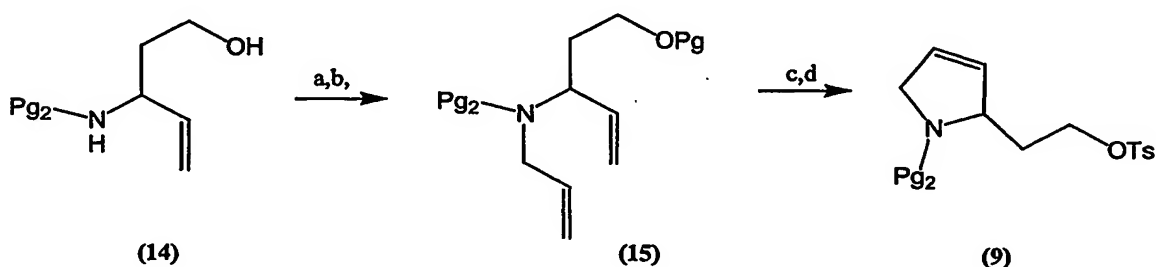
15

Treatment of the methyl ester (8) with a reducing agent such as DIBAL-H (diisobutylaluminium hydride) provides the primary alcohol, which is readily converted to tosylate (9). Similarly the mesylate or triflate analogues of (9) may be prepared. Nucleophilic displacement of the activated alcohol with sodium azide provides intermediate (10) e.g. 2-(2-Azido-ethyl)-2,5-dihydro-pyrrole-1-carboxylic acid tert-butyl ester. Epoxidation of (10) with oxidising agents common to the art such as *m*-CPBA provides the epoxide (11) e.g. 2-(2-Azido-ethyl)-6-oxa-3-aza-bicyclo[3.1.0]hexane-3-carboxylic acid tert-butyl ester. Reduction of the azide (11) to the amine intermediate may be effected under a

20

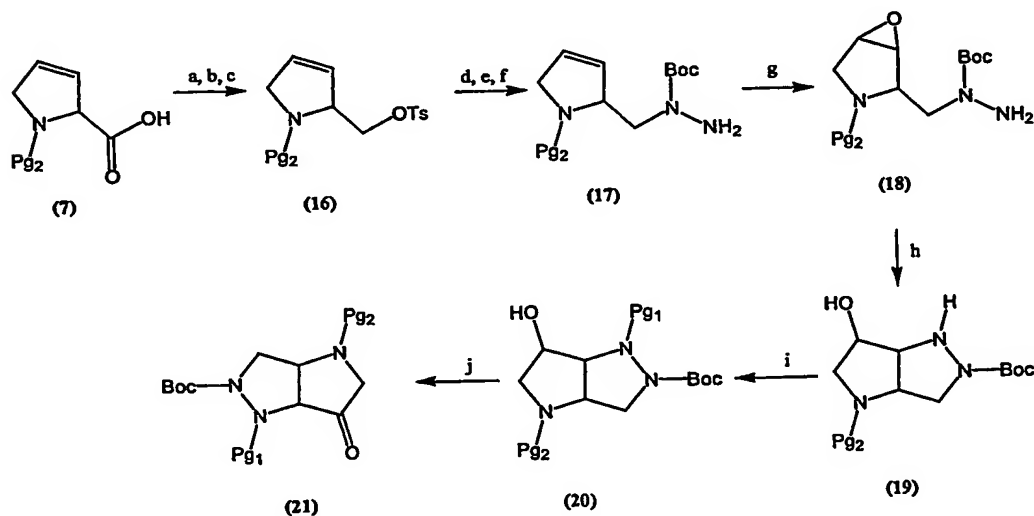
range of conditions such as Pd-C / H₂ or triphenylphosphine in THF and water. The amine intermediates undergo intramolecular epoxide ring opening to provide the bicyclic alcohol (12) e.g. 3-Hydroxy-hexahydro-pyrrolo[3,2-b]pyrrole-1-carboxylic acid tert-butyl ester. The free secondary amine (12) may be protected with a variety of suitable protecting groups such as Fmoc, Boc, Cbz, Alloc to provide orthogonal protection of the bicyclic scaffold. Protected alcohol (13) may be oxidised by reagents common to the art such as pyridine sulphur trioxide complex in DMSO and triethylamine or Dess-Martin periodane to provide ketone (6) e.g. 3-Oxo-hexahydro-pyrrolo[3,2-b]pyrrole-1,4-dicarboxylic acid 1-tert-butyl ester 4-(9H-fluoren-9-ylmethyl) ester.

Alternative routes towards intermediate (9) (ex Scheme 2) are available such as that detailed in Scheme 3. Protected alkene (14) is readily available following literature procedures from the protected homoserine lactol ((a) Wright, D. L. *et al*, *Org. Lett.*, 2(13), 1847-1850, 2000. (b) Boyle, P. H. *et al*, *Tet. Asymm.*, 6, 2819, 1995. (c) Baldwin, J. E. and Flinn, A., *Org. Lett.*, 28, 3605, 1987.). N-alkylation of (14) with a base such as sodium hydride and allyl bromide provides diene (15). Treatment of (15) with the olefin metathesis catalysts developed by Grubbs such as bis(tricyclohexylphosphine)benzylidene ruthenium (IV) dichloride provides the protected primary alcohol intermediate of compound (9) detailed in Scheme 2.



Scheme 3. (a) Primary alcohol protection, e.g. TBDMS-Cl, base (b) NaH, allylbromide, DMF. (c) bis(tricyclohexylphosphine)benzylidene ruthenium (IV) dichloride, DCM, reflux (d) i. TBAF, THF, ii. Tosylchloride, pyridine.

The hexahydropyrrolo[3,2-*c*]pyrazol-6-one (21) scaffold may be prepared following a similar route to that described in Scheme 2 (see Scheme 4). Treatment of the protected 3,4-dehydropoline (7) with HCl in methanol provides the methyl ester. Reduction of the ester with a reducing agent such as DIBAL-H (diisobutylaluminium hydride) provides the primary alcohol, which is readily converted to tosylate (16). Similarly the mesylate or triflate analogues of (16) may be prepared. Nucleophilic displacement of the activated alcohol with a protected hydrazide e.g. Hydrazinecarboxylic acid allyl ester (Alloc-NHNH₂) followed by Boc protection of the secondary hydrazide e.g. under standard Schotten-Baumann conditions and removal of the alloc group e.g. (PPh₃)₄Pd⁰ / DCM / PhSiH₃ provides (17). Epoxidation of (17) with oxidising agents common to the art such as *m*-CPBA provides the epoxide intermediate (18). Intermediate (18) readily undergoes intramolecular epoxide ring opening to provide the bicyclic alcohol (19). The free secondary hydrazide (19) may be protected with a variety of suitable protecting groups e.g. Fmoc, Cbz, Alloc to provide orthogonal protection of the bicyclic scaffold. Protected alcohol (20) may be oxidised by reagents common to the art such as pyridine sulphur trioxide complex in DMSO and triethylamine or Dess-Martin periodane to provide ketone (21).

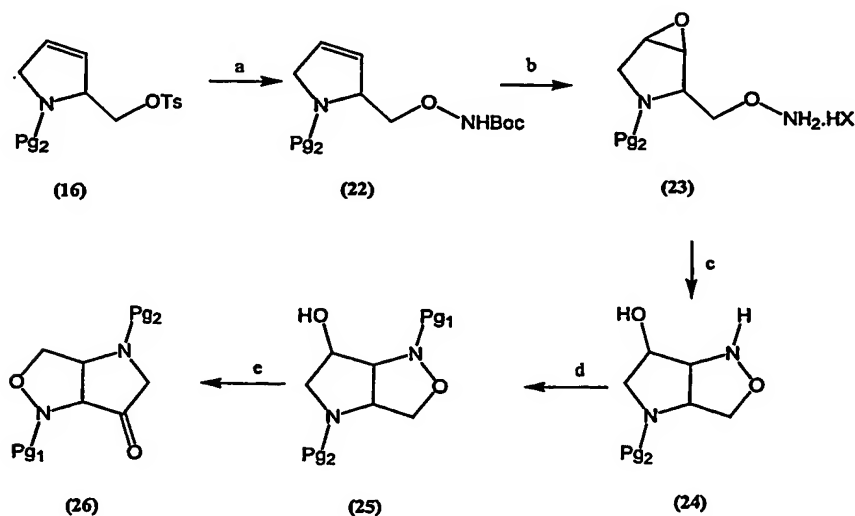


Scheme 4. (a) MeOH / HCl, Dean-Stark (b) DIBAL reduction. (c) Tosylchloride, pyridine (d) Alloc-NHNH₂ (e) (Boc)₂O, Na₂CO₃, dioxan, water (f) (PPh₃)₄Pd⁰ / DCM / PhSiH₃ (g) *m*-

-101-

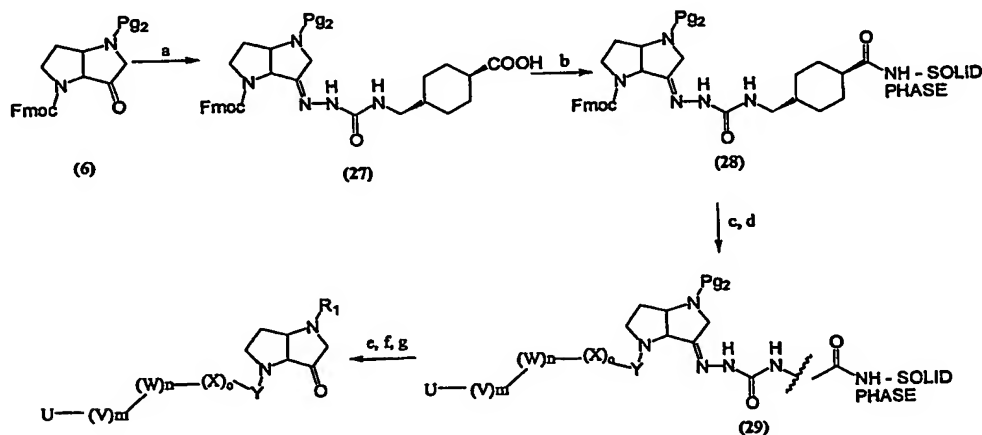
chloroperbenzoic acid, DCM. (h) Δ (i) Pg₁ protection, e.g. 1.05 eq Fmoc-Cl, 2.1eq Na₂CO₃, dioxan, water. (j) Dess-Martin periodane, DCM.

The hexahydro-2-oxa-1,4-diazapentalen-6-one (26) scaffold may be prepared following a similar route to that described in Scheme 4. Tosylate (16) undergoes nucleophilic displacement with a protected oxyamine e.g. N-Boc hydroxylamine to provide intermediate (22). Epoxidation of (22) with oxidising agents common to the art such as *m*-CPBA provides the epoxide intermediate, which upon acidolytic removal of the Boc group provides intermediate amine.salt (23). Neutralisation of the amine.salt initiates intramolecular epoxide ring opening to provide the bicyclic alcohol (24). The free secondary amine (24) may be protected with a variety of suitable protecting groups e.g. Fmoc, Cbz, Alloc, Boc to provide orthogonal protection of the bicyclic scaffold. Protected alcohol (25) may be oxidised by reagents common to the art such as pyridine sulphur trioxide complex in DMSO and triethylamine or Dess-Martin periodane to provide ketone (26) e.g. 6-Oxo-tetrahydro-2-oxa-1,4-diaza-pentalene-1,4-dicarboxylic acid 4-benzyl ester 1-(9H-fluoren-9-ylmethyl) ester.



Scheme 5. (a) Boc-NHOH (b) i. *m*-chloroperbenzoic acid, DCM. ii. e.g. HCl / dioxan. (c) Base neutralisation e.g. N-methylmorpholine in DMF. (d) Pg₁ protection, e.g. 1.05 eq Fmoc-Cl, 2.1eq Na₂CO₃, dioxan, water. (e) Dess-Martin periodane, DCM.

The protected building blocks detailed in Schemes 1, 2, 4 and 5 may be utilised in a solid phase synthesis of inhibitor molecules (steps (b) to (e)). Preferred protecting group combinations include 'Pg₁' = Fmoc / 'Pg₂' = Boc, or 'Pg₁' = Fmoc / 'Pg₂' = Alloc, or 'Pg₁' = Boc / 'Pg₂' = Fmoc, or 'Pg₁' = Boc / 'Pg₂' = Alloc, or 'Pg₁' = Alloc / 'Pg₂' = Fmoc, or 'Pg₁' = Alloc / 'Pg₂' = Boc. The solid phase syntheses exemplified in Schemes 6 and 7 by the use of hexahydropyrrolo[3,2-*b*]pyrrol-3-one (6) and octahydropyrrolo[3,2-*b*]pyrrol-3-ol (13) could equally apply to ketones (21) and (26) and alcohols (20) and (25). Step (b), the solid phase linkage of an aldehyde or ketone, has previously been described by a variety of methods (e.g. see (a) James, I. W., 1999, (b) Lee, A., Huang, L., Ellman, J. A., *J. Am. Chem. Soc.*, 121(43), 9907-9914, 1999, (c) Murphy, A. M., *et al*, *J. Am. Chem. Soc.*, 114, 3156-3157, 1992). A suitable method amenable to the reversible linkage of an alkyl ketone functionality such as (6) is through a combination of the previously described chemistries. The semicarbazide, 4-[[[(hydrazinocarbonyl)amino]methyl]cyclohexane carboxylic acid. trifluoroacetate (Murphy, A. M., *et al*, *J. Am. Chem. Soc.*, 114, 3156-3157, 1992), may be utilised as illustrated in Scheme 6, where 'Pg₁' = Fmoc and 'Pg₂' = Boc or Alloc, exemplified by linkage of the hexahydropyrrolo[3,2-*b*]pyrrol-3-one (6).



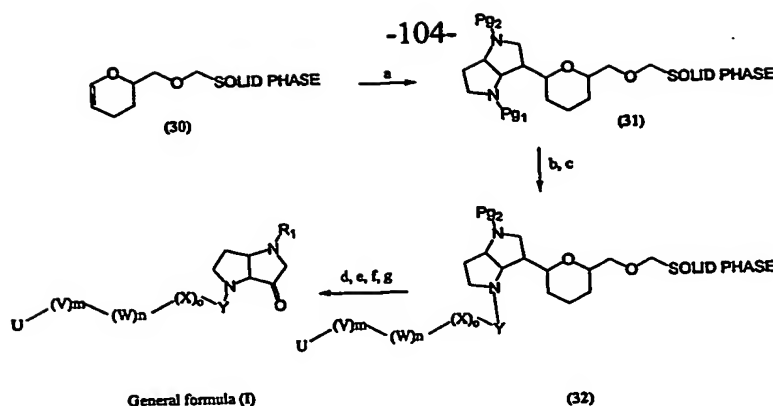
General formula (I)

-103-

Scheme 6. (a) (6) in 90% EtOH / H₂O / NaOAc / 4-[[[(hydrazinocarbonyl)amino]methyl]-cyclohexane carboxylic acid.trifluoroacetate, reflux. (b) 3eq construct (27) / 3eq HBTU / 3eq HOBT / 6eq NMM, NH₂-SOLID PHASE, DMF, RT, o/n. (c) 20% piperidine / DMF, RT, 30mins. (d) Range of chemistries to add U-V-W-X-Y. (e) 'Pg₂' = Boc then 50%TFA in DCM, or 'Pg₂' = Alloc then e.g. (PPh₃)₄Pd(0) catalysed deprotection /CHCl₃ / DMF / AcOH / NMM (f) i. RCOOH / activation e.g. HBTU / HOBT / NMM, in DMF or ii. SO₂Cl, pyridine in DMF. (g) 95% TFA / H₂O.

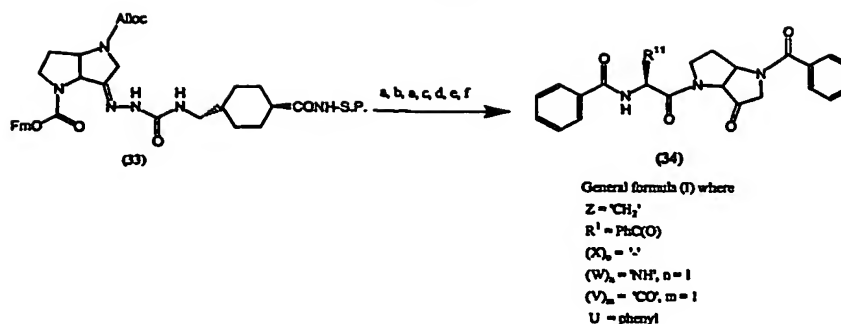
Construct (28) is prepared through reaction of the linker molecule (27) and the hexahydropyrrolo[3,2-*b*]pyrrol-3-one (6) by reflux in aqueous ethanol / sodium acetate. Standard solid phase techniques (e.g. see Atherton, E. and Sheppard, R. C. In '*Solid Phase Peptide Synthesis: A Practical Approach*', Oxford University Press, Oxford, U.K. 1989) are used to anchor the construct to an amino-functionalised solid phase through the free carboxylic acid functionality of (27), providing the loaded construct (28). Loaded construct (28) may be reacted with a wide range of carboxylic acids or sulphonyl chlorides available commercially in the literature, to introduce the left-hand portion 'U-V-W-X-Y' in general formula (I), providing loaded construct (29). Orthogonal removal of 'Pg₂' then liberates the secondary amine functionality of the right-hand ring, which may be acylated with a range of carboxylic acid and sulphonyl chlorides. Finally, compounds of general formula (I) are released from the solid phase by treatment with 95% aq trifluoroacetic acid.

An alternative solid phase synthesis of compounds of general formula (I) utilises the bicyclic alcohol intermediate (13), Scheme 7. The secondary alcohol may be attached to the solid phase through the acid labile dihydropyran linker (30) that is well known in the literature (e.g. see (a) Thompson, L. A. and Ellman, J. A., *Tet. Lett.*, **35**, 9333, 1994. (b) Kick, E. K. and Ellman, J. A. *J. Med. Chem.*, **38**, 1427, 1995.). Preferred protecting group combinations include 'Pg₁' = Fmoc / 'Pg₂' = Alloc, or 'Pg₁' = Alloc / 'Pg₂' = Fmoc.



- Scheme 7. (a) (13) in dichloroethane, pyridinium p-toluenesulphonate, reflux (b) 'Pg₁' = Fmoc then 20% piperidine / DMF, RT, 30mins or 'Pg₁' = Alloc then (PPh₃)₄Pd(0) catalysed deprotection /CHCl₃ / DMF / AcOH / NMM (c) Range of chemistries to add U-V-W-X-Y. (d) 'Pg₂' = Fmoc then 20% piperidine / DMF, RT, 30mins or 'Pg₂' = Alloc then e.g. (PPh₃)₄Pd(0) catalysed deprotection /CHCl₃ / DMF / AcOH / NMM (e) i. RCOOH / activation e.g. HBTU / HOBT / NMM, in DMF or ii. SO₂Cl, pyridine in DMF. (f) 95% TFA / H₂O. (g) Solid supported oxidation or e.g. Dess-Martin periodane, DCM.
- 10 Loaded construct (31) may be reacted with a wide range of carboxylic acids or sulphonyl chlorides available commercially in the literature, to introduce the left-hand portion 'U-V-W-X-Y' in general formula (I), providing loaded construct (32). Orthogonal removal of 'Pg₂' then liberates the secondary amine functionality of the right-hand ring, which may be acylated with a range of carboxylic acid and
- 15 sulphonyl chlorides. Compounds of general formula (I) are released from the solid phase by treatment with 95% aq trifluoroacetic acid and the resultant alcohols may be oxidised with a range of solution based reagents e.g. Dess-Martin periodane in DCM or solid supported oxidants (e.g. see Ley, S. V. *et al*, *J. Chem. Soc. Perkin Trans. 1.*, 3815-4195, 2000.) to provide the ketone products.
- 20 In the simplest example, the entire left hand portion of an inhibitor of general formula (I) comprises a capped aminoacid (Scheme 8), providing for example analogues of general formula (I) where Z = 'CH₂', Y = CHR¹⁸C(O), (X)₀ = '-', (W)_n = 'NH', R¹⁸ = 'H', n = 1, (V)_m = 'CO', m = 1 and U = phenyl. Scheme 8
- 25 details chemistry utilising protected ketone construct (33) and the reactions could equally be applied to the protected alcohol construct (31).

-105-

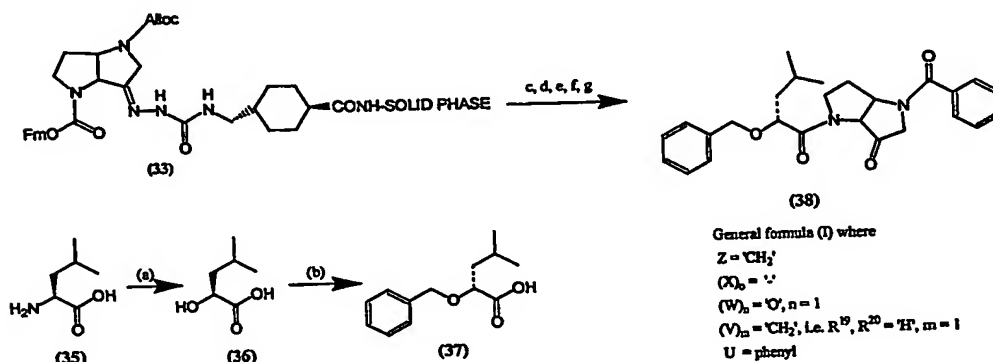


Scheme 8. (a) 20% piperidine / DMF, 30mins (b) 20eq Fmoc-aminoacid / 20eq HBTU / 20eq HOBt / 40eq NMM, DMF, o/n (c) 5eq carboxylic acid / 5eq HBTU / 5eq HOBt / 10eq NMM, DMF, RT, o/n (d) Deprotection of Pg₂ Alloc; e.g. TMS-N₃ / TBAF / (PPh₃)₄Pd⁰ / under N₂. (e) 20eq Benzoic acid / 20eq HBTU / 20eq HOBt / 40eq NMM, DMF, RT, o/n (f) TFA / H₂O (95:5, v/v), RT.

Alternatively, carboxylic acids can be prepared in solution by traditional organic chemistry methods and coupled to constructs (28) and (31) on the solid phase (Schemes 9-13). For example (Scheme 9), treatment in solution of an amino acid, exemplified by (35) with sodium nitrite / H₂SO₄, provides the α -hydroxyacid, exemplified by (36) (Degerbeck, F. *et al*, *J. Chem. Soc, Perkin Trans. 1*, 11-14, 1993). Treatment of α -hydroxyacid, (36) with sodium hydride in a dimethylformamide / dichloromethane mixture followed by addition of benzyl bromide, provides (*RS*) 2-benzyloxy-4-methyl-pentanoic acid (37). Coupling of (37) to the solid phase construct (33) followed by alloc deprotection, benzoylation then cleavage, provides (38), an example of general formula (I) where $Z = \text{'CH}_2\text{'}$, $(X)_0 = \text{'- '}$, $(W)_n = \text{'O'}$, $n = 1$, $(V)_m = \text{'CH}_2\text{'}$, $m = 1$, R^{19} and $R^{20} = \text{H}$ and $U = \text{phenyl}$. To those skilled in the practices of organic synthesis, a wide variety of aminoacids such as (35) may be converted to the corresponding α -hydroxyacid such as (36) following the general conditions detailed. Additionally, benzylbromide may be replaced by any reasonable Ar-CR¹⁹R²⁰-halide, providing many variations of carboxylic acid (37) following the general conditions detailed. In certain instances, it may be advantageous to temporarily protect the carboxylic acid as the methyl ester (for example compound (43), Scheme 11) prior to reaction with the alkylhalide. The ester intermediate is then simply hydrolysed to

-106-

acid (37). Analogues of (38), exploring a wide range of (V)_m and U in general formula (I) may be prepared through the general conditions detailed in Scheme 9.



5 Scheme 9. (a) NaNO₂ / H₂SO₄, 0°C → RT, 2hr (b) 2.3eq NaH, 1:1 DMF / DCM, 1.4eq benzylbromide, o/n (c) 20% piperidine / DMF, 30mins. (d) 10eq (37) / 10eq HBTU / 10eq HOBt / 20eq NMM, DMF, RT, o/n (e) Deprotection of Pg₂ Alloc; e.g. TMS-N₃ / TBAF / (PPh₃)₄Pd⁰ / under N₂. (f) 20eq Benzoic acid / 20eq HBTU / 20eq HOBt / 40eq NMM, DMF, RT, o/n (g) TFA / H₂O (95:5, v/v), RT.

10

Since the final synthetic step involves a trifluoroacetic acid (TFA) mediated cleavage of the solid phase bound compound, analogues where the substituted ether is labile to TFA may be prepared in solution by an alternative route (see Scheme 16).

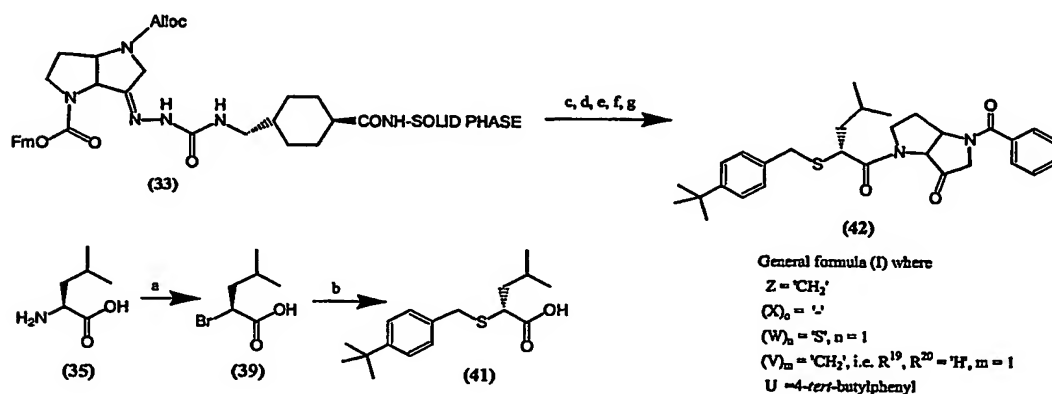
15

Alternatively, coupling of construct (33) (following removal of Fmoc) with the α-hydroxyacid (36), provides a versatile solid phase bound intermediate 'Y' substituent in general formula (I) that may be reacted with many reagents. For example, the α-hydroxyl can be reacted under Mitsunobu conditions (Hughes, D. L. *Org. React. (N.Y.)*, 42, 335-656, 1992) to give ethers (i.e. X = '-', W = 'O', in general formula (I)) (see Grabowska, U. *et al*, *J. Comb. Chem.*, 2(5), 475-490, 2000, for an example of Mitsunobu reaction on the solid phase). Alternatively, the α-hydroxyl can be reacted with a carbamoyl chloride to give a carbamate (i.e. X = '-', W = 'O', V = 'NHC(O)', in general formula (I)).

25

-107-

Alternatively, (Scheme 10), treatment in solution of an amino acid, exemplified by (35) with sodium nitrite / H₂SO₄ / potassium bromide provides the α -bromoacid, exemplified by (39) (Souers, A. J. *et al*, *Synthesis*, 4, 583-585, 1999) with retention of configuration. Treatment of α -bromoacid (39) with an alkylthiol exemplified by 4-*tert*-butylphenylmethanethiol (40) in dimethylformamide / triethylamine, provides 2*R*-(4-*tert*-butylbenzylsulfanyl)-4-methylpropionic acid (41), with inversion of configuration. Coupling of (41) to the solid phase construct (33) followed by alloc deprotection, benzylation, then cleavage provides (42), an example of general formula (I) where Z = 'CH₂', (X)₀ = '-', (W)_n = 'S', n = 1, (V)_m = 'CH₂', m = 1, R¹⁹ and R²⁰ = H and U = 4-*tert*-butylphenyl. To those skilled in the practices of organic synthesis, a wide variety of aminoacids such as (35) may be converted to the corresponding α -bromoacid such as (39) following the general conditions detailed. Additionally, starting with the *R*-isomer of (35) gives the *R*-bromoacid analogue of (39) and *S*-thioether analogue of (41). Additionally, (4-*tert*-butylphenyl)methanethiol (40) may be replaced by any reasonable Ar-CR¹⁹R²⁰-SH, providing many variations of carboxylic acid (41) following the general conditions detailed. Thus analogues of (42) exploring a wide range of (V)_m and U in general formula (I) may be prepared through the general conditions detailed in Scheme 10.



Scheme 10. (a) NaNO₂ / H₂SO₄, KBr 0°C → RT, 2hr (b) Alkylthiol (40) / DMF / NEt₃, o/n (c) 20% piperidine / DMF, 30mins. (d) 10eq (41) / 10eq HBTU / 10eq HOBt / 20eq NMM, DMF, RT, o/n

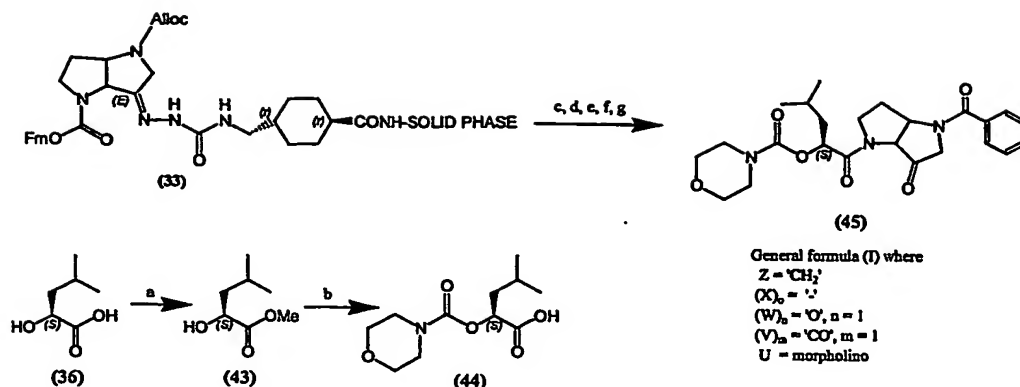
-108-

(e) Deprotection of Pg₂ Alloc; e.g. TMS-N₃ / TBAF / (PPh₃)₄Pd⁰ / under N₂. (f) 20eq Benzoic acid / 20eq HBTU / 20eq HOBt / 40eq NMM, DMF, RT, o/n (g) TFA / H₂O (95:5, v/v), RT.

Alternatively, coupling of construct (33) (following removal of Fmoc) with an α -bromoacid e.g. (39), provides a versatile intermediate 'Y' substituent in general formula (I) that may be reacted with many reagents. For example, the α -bromide can be displaced with nucleophiles e.g. alcohols, thiols, carbanions etc, to give ethers (i.e. X = '-', W = 'O', in general formula (I)), thioethers (i.e. X = '-', W = 'S', in general formula (I)). The thioethers may optionally be oxidised to the sulphone (see Scheme 14, i.e. X = '-', W = 'SO₂', in general formula (I)) (see Grabowska, U. *et al*, *J. Comb. Chem.*, 2(5), 475-490, 2000, for an example of bromide displacement and thioether oxidation on the solid phase).

Alternatively, (Scheme 11), treatment of an α -hydroxyacid, exemplified by (36) with trimethylsilylchloride and methanol provides the methyl ester (43). Activation of the free hydroxyl to the chloroformate with phosgene in dichloromethane followed by addition of morpholine, then hydrolysis, provides morpholine-4-carboxylic acid 1-carboxy-3-methyl-butyl ester (44). Coupling of (44) to the solid phase construct (33) followed by alloc deprotection, benzylation then cleavage provides (45), an example of general formula (I) where Z = 'CH₂', (X)_o = '-', (W)_n = 'O', n = 1, (V)_m = 'CO' and U = morpholino. To those skilled in the practices of organic synthesis, a wide variety of α -hydroxyacid esters such as (36) could be converted to the activated chloroformate following the general conditions detailed. Additionally, morpholine may be replaced by any reasonable amine, providing many variations of carboxylic acid (44) following the general conditions detailed. Thus analogues of (45) exploring a wide range of (V)_m and U in general formula (I) may be prepared through the general conditions detailed in Scheme 11.

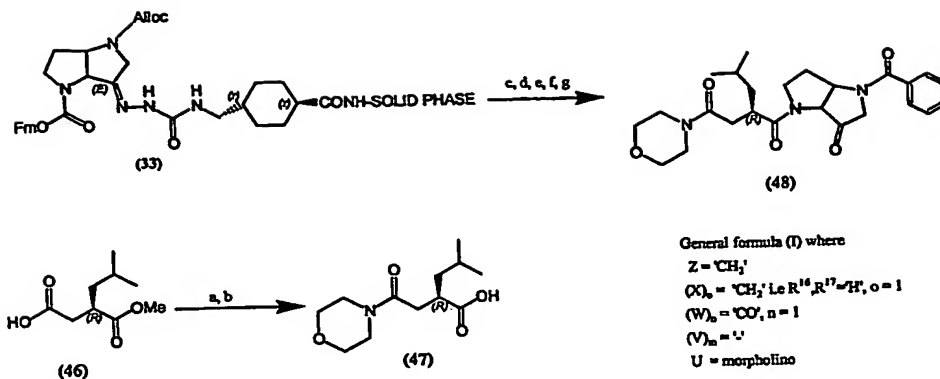
-109-



Scheme 11. (a) Me_3SiCl , MeOH , RT, o/n. (b) i. COCl_2 / DCM / o/n, ii. Morpholine / DCM 0°C , 2hr, iii. LiOH in H_2O / dioxan, 0°C . (c) 20% piperidine / DMF , 30mins. (d) 10eq (44) / 10eq HBTU / 10eq HOBt / 20eq NMM, DMF , RT, o/n. (e) Deprotection of Pg_2 Alloc; e.g. TMS-N_3 / TBAF / $(\text{PPh}_3)_4\text{Pd}^0$ / under N_2 . (f) 20eq Benzoic acid / 20eq HBTU / 20eq HOBt / 40eq NMM, DMF , RT, o/n. (g) TFA / H_2O (95:5, v/v), RT.

Alternatively, (Scheme 12), a wide range of alkylsuccinate esters exemplified by 2*R*-isobutyl-succinic acid 1-methyl ester (46) are commercially available or readily prepared by known methods (see (a) Azam *et al*, *J. Chem. Soc. Perkin Trans. 1*, 621-, 1996; (b) Evans *et al*, *J. Chem. Soc. Perkin Trans. 1*, 103, 2127, 1981; (c) Oikawa *et al*, *Tet. Lett.*, 37, 6169, 1996). Carboxyl activation of alkylsuccinate ester (46) followed by addition of morpholine in dimethylformamide and subsequent ester hydrolysis, provides 4-Methyl-2*R*-(2-morpholin-4-yl-2-oxo-ethyl)-pentanoic acid (47). Coupling of (47) to the solid phase construct (33) followed by alloc deprotection, benzylation then cleavage provides (48), an example of general formula (I) where $Z = \text{'CH}_2\text{'}$, $(X)_o = \text{'CH}_2\text{'}$, $(W)_n = \text{'CO'}$, $n = 1$, $(V)_m = \text{'-'}\text{'}$ and $U = \text{morpholino}$. To those skilled in the practices of organic synthesis, a wide variety of alkylsuccinate esters such as (46) may be prepared and converted to the corresponding substituted alkylsuccinate acid such as (47) following the general conditions detailed. Additionally, morpholine may be replaced by any reasonable amine, providing many variations of carboxylic acid (47) following the general conditions detailed. Thus analogues of (48) exploring a wide range of $(X)_o$, $(V)_m$ and U in general formula (I) may be prepared through the general conditions detailed in Scheme 12.

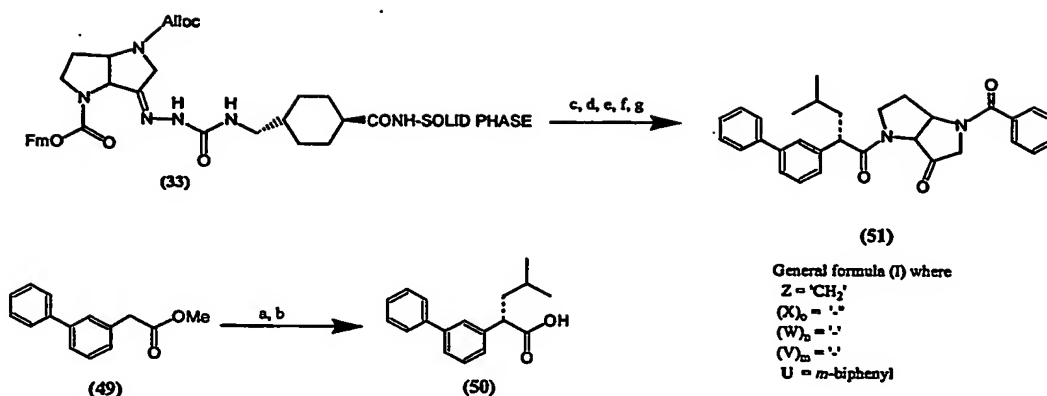
-110-



Scheme 12. (a) i.EDC / 1-hydroxybenzotriazole /DMF, 0°C, 30mins. ii. Morpholine, RT, o/n (b) LiOH in H₂O / dioxan, 0°C (c) 20% piperidine / DMF, 30mins. (d) 10eq (47) / 10eq HBTU / 10eq HOBt / 20eq NMM, DMF, RT, o/n. (e) Deprotection of Pg₂ Alloc; e.g. TMS-N₃ / TBAF / (PPh₃)₄Pd⁰ / under N₂. (f) 20eq Benzoic acid / 20eq HBTU / 20eq HOBt / 40eq NMM, DMF, RT, o/n. (g) TFA / H₂O (95:5, v/v), RT.

Alternatively, (Scheme 13), a wide range of biarylalkylacetic acids, exemplified by 2*RS*-biphenyl-3-yl-4-methylpentanoic acid (50) are readily available by known methods (see (a) DesJarlais, R. L. *et al*, *J. Am. Chem. Soc.*, **120**, 9114-9115, 1998; (b) Oballa, R. M. *et al*, WO 0149288). Coupling of biarylalkylacetic acid (50) to the solid phase construct (33) followed by alloc deprotection, benzoylation then cleavage provides (51), an example of general formula (I) where Z = 'CH₂', (X)_n = '-', (W)_n = '-', (V)_m = '-' and U = *m*-biphenyl. To those skilled in the practices of organic synthesis, a wide variety of biarylalkylacetic acids such as (50) may be prepared by alkylation of the α-anion of the free acid analogue of (49), which in turn is prepared by Suzuki coupling of phenylboronic acid and 3-bromophenylacetic acid methyl ester. Phenylboronic acid may be replaced by a wide range of arylboronic acids in the Suzuki coupling, providing many variations of carboxylic acid (50) following the general conditions detailed. Thus analogues of (51) exploring a wide range of group 'U' in general formula (I) may be prepared through the general conditions detailed in Scheme 13.

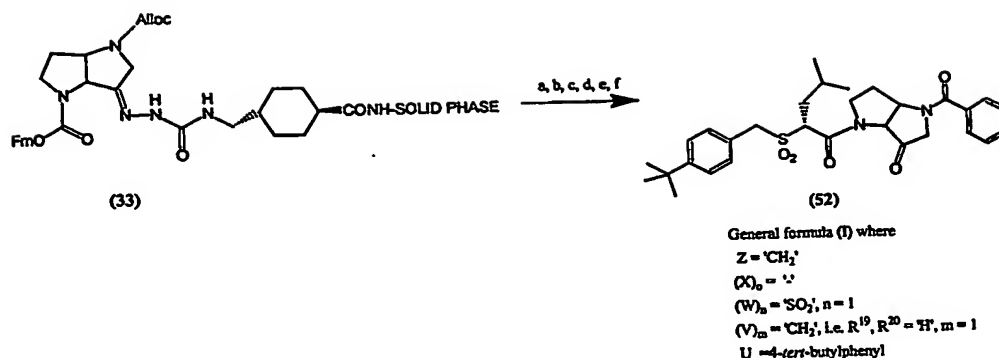
-111-



Scheme 13. (a) LiOH in H₂O / dioxan, 0°C (b) i.LDA, THF, 2-methylpropenylbromide. ii. Pd/C, EtOH, H₂ (c) 20% piperidine / DMF, 30mins. (d) 10eq (50) / 10eq HBTU / 10eq HOBT / 20eq NMM, DMF, RT, o/n. (e) Deprotection of Pg₂ Alloc; e.g. TMS-N₃ / TBAF / (PPh₃)₄Pd⁰ / under N₂. (f) 20eq Benzoic acid / 20eq HBTU / 20eq HOBT / 40eq NMM, DMF, RT, o/n. (g) TFA / H₂O (95:5, v/v), RT.

Many other possibilities for solid phase organic chemistry (e.g. see Brown, R. D. *J. Chem. Soc., Perkin Trans.1*, **19**, 3293-3320, 1998, for a review of recent SPOC publications) can be used to derivatise constructs (28) and (31) towards compounds of general formula (I). For example, the left-hand portion 'U-V-W-X-Y' in general formula (I) can be partially constructed in solution, coupled to constructs (28) and (31) and further modified on the solid phase. For example (Scheme 14), a simple extension of Scheme 10 is through the oxidation of the intermediate solid phase bound species, with *m*-chloroperbenzoic acid in dichloromethane prior to cleavage, to give the sulphone analogue. Commencing from 2*R*-(4-*tert*-butylbenzylsulfanyl)-4-methylpropionic acid (41), sulphone (52) is prepared, an example of general formula (I) where Z = 'CH₂', (X)₀ = '-', (W)_n = 'SO₂', n = 1, (V)_m = 'CH₂', m = 1, R¹⁹ and R²⁰ = H and U = 4-*tert*-butylphenyl. As described in Scheme 10, many variations of carboxylic acid (41) may be prepared following the general conditions detailed. Thus analogues of (52) exploring a wide range of (V)_m and U in general formula (I) may be prepared through the general conditions detailed in Schemes 10 and 14.

-112-



Scheme 14. (a) 20% piperidine / DMF, 30mins. (b) 10eq (41) / 10eq HBTU / 10eq HOBT / 20eq NMM, DMF, RT, o/n. (c) Deprotection of Pg₂ Alloc; e.g. TMS-N₃ / TBAF / (PPh₃)₄Pd⁰ / under N₂. (d) 20eq Benzoic acid / 20eq HBTU / 20eq HOBT / 40eq NMM, DMF, RT, o/n. (e) 5eq *m*-chloroperbenzoic acid / DCM, RT, 5hr. (f) TFA / H₂O (95:5, v/v), RT.

Compounds of general formula (I) are finally released from the solid phase by treatment with trifluoroacetic acid / water, followed by evaporation, lyophilis and standard analytical characterisation.

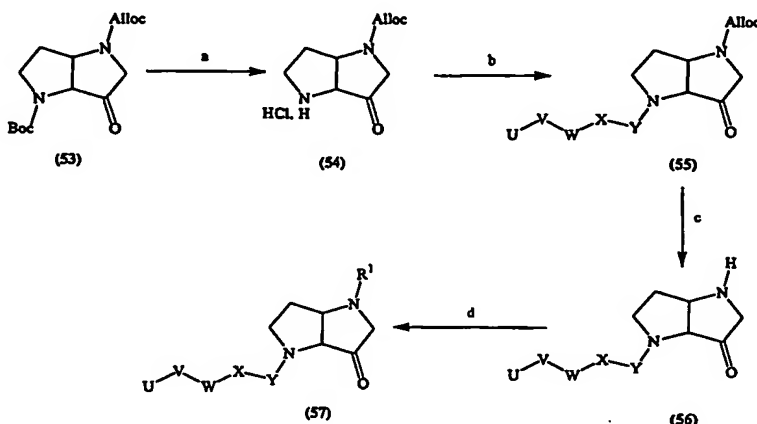
A second strategy for the synthesis of compounds of general formula (I) comprises:-

(a) Preparation of an appropriately functionalised and protected hexahydropyrrolo[3,2-*b*]pyrrol-3-one, hexahydropyrrolo[3,2-*c*]pyrazol-6-one or hexahydro-2-oxa-1,4-diazapentalen-6-one building block in solution.

Preferred protecting groups for solution phase chemistry are the 9-fluorenylmethoxycarbonyl, *N*α-*tert*-butoxycarbonyl, *N*α-benzyloxy carbonyl and *N*α-allyloxycarbonyl group.

(b) Standard organic chemistry methods for the conversion of building block (a) towards compounds of general formula (I).

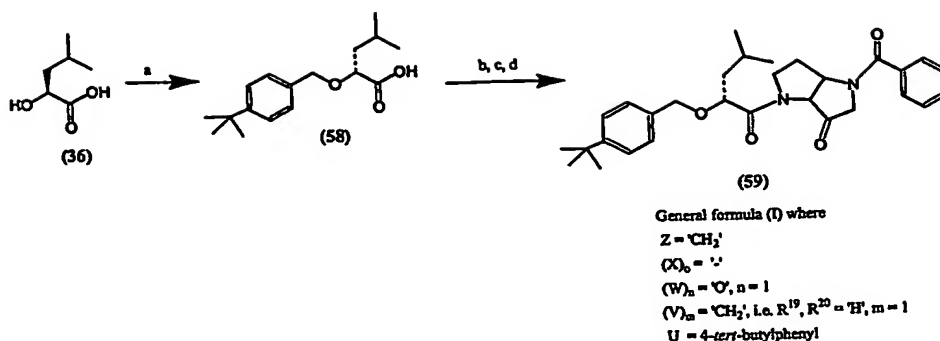
In the simplest example, the entire left hand portion of an inhibitor of general formula (I) can be prepared in solution by traditional organic chemistry methods and coupled to building block (a) (see Scheme 15 exemplified by the use of 3-Oxo-hexahydro-pyrrolo[3,2-b]pyrrole-1-carboxylic acid allyl ester (54)).



Scheme 15. (a) 4M HCl in dioxan, 0°C. (b) Pre-prepared U-V-W-X-Y-COOH / activation e.g. HATU / HOAt / NMM, DMF, RT, o/n. (c) Alloc deprotection e.g. (PPh₃)₄Pd⁰ / DCM / PhSiH₃ (d) Acylation e.g. RCOOH, ^tBuOCOCl, NMM, DCM, or SO₂Cl / Pyridine.

- 5
- 10 The general strategy detailed in Scheme 15 is particularly useful when the compound of general formula (I) contains a substituent that is labile to trifluoroacetic acid, this being the final reagent used in each of the solid phase Schemes 6-14. For example (Scheme 16), treatment in solution of α -hydroxyacid (36) with sodium hydride in a dimethylformamide / dichloromethane mixture
- 15 followed by addition of 4-*tert*-butylbenzyl bromide, provides 2*RS*-(4-*tert*-butylbenzyloxy)-4-methylpentanoic acid (58). Coupling of (58) to hydrochloride salt (54), followed by alloc deprotection then benzylation provides (59), an example of general formula (I) where Z = 'CH₂', (X)₀ = '-', (W)_n = 'O', n = 1, (V)_m = 'CH₂', m = 1, R¹⁹ and R²⁰ = H and U = 4-*tert*-butylphenyl. To those skilled
- 20 in the practices of organic synthesis, 4-*tert*-butylbenzyl bromide may be replaced by any reasonable Ar-CR¹⁹R²⁰-halide, providing many variations of carboxylic acid (58) under the conditions shown. Thus analogues of (59) exploring a wide range of (V)_m and U in general formula (I) may be prepared through the conditions detailed in Scheme 16.

-114-



5 Scheme 16. (a) 2.2eq NaH, 1:1 DMF / DCM, 1.25eq 4-*tert*-benzylbromide. (b) 1eq (58), 1eq $t\text{-BuOCOC}$ l, 2eq NMM, DCM, -15°C , 1hr, under nitrogen, then 1eq, (54), RT, o/n. (c) Alloc deprotection e.g. $(\text{PPh}_3)_4\text{Pd}^0$ / DCM / PhSiH_3 (d) Acylation e.g. RCOOH , $t\text{-BuOCOC}$ l, NMM, DCM, or SO_2Cl / Pyridine.

10 A third strategy for the synthesis of compounds of general formula (I) where the addition of U-V-W-X-Y to the protected building block involves multistep organic reactions comprises:-

15 (a) Preparation of an appropriately functionalised and protected hexahydropyrrolo[3,2-*b*]pyrrol-3-one, hexahydropyrrolo[3,2-*c*]pyrazol-6-one or hexahydro-2-oxa-1,4-diazapentalen-6-one building block in solution.

Preferred protecting groups for solution phase chemistry are the 9-fluorenylmethoxycarbonyl, $N\alpha$ -*tert*-butoxycarbonyl, $N\alpha$ -benzyloxy carbonyl and $N\alpha$ -allyloxycarbonyl group.

20 (b) Protection of the ketone functionality of the hexahydropyrrolo[3,2-*b*]pyrrol-3-one, hexahydropyrrolo[3,2-*c*]pyrazol-6-one or hexahydro-2-oxa-1,4-diazapentalen-6-one building block e.g. as a dimethylacetal. Alternatively, the reduced ketone (achiral secondary alcohols (13), (20) and (25)) intermediates may be used and re-oxidised as the final synthetic

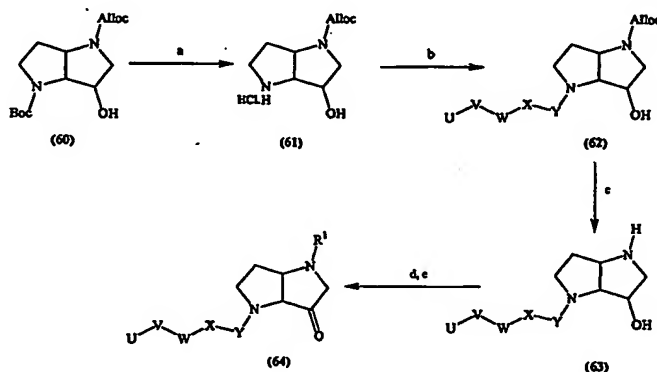
25

step.

- (c) Standard organic chemistry methods for the conversion of building block (b) towards compounds of general formula (I).

5

Intermediates may be prepared in solution, followed by coupling to building block (b) and further derivitisation towards compounds of general formula (I) (see Scheme 17 exemplified by preparation and use of the 3-Hydroxy-hexahydro-pyrrolo[3,2-b]pyrrole-1-carboxylic acid allyl ester (61)).



10

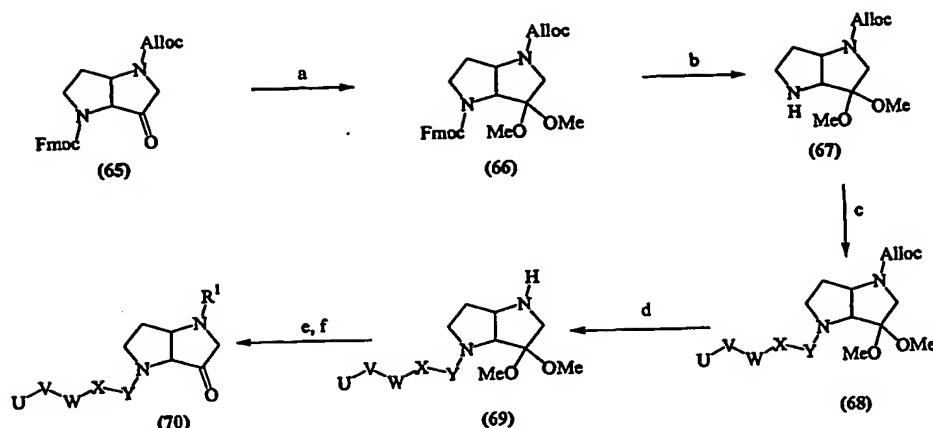
Scheme 17. (a) 4M HCl in dioxan, 0°C. (b) Stepwise reaction with intermediates of Y, then X, then W etc., to stepwise construct compounds (62). (c) Alloc deprotection e.g. $(PPh_3)_4Pd^0$ / DCM / $PhSiH_3$ (d) Acylation e.g. $RCOOH$, $tBuOCOCl$, NMM, DCM, or SO_2Cl_2 / Pyridine. (e) Oxidation, e.g. Dess-Martin periodane, CH_2Cl_2 .

15

Alternatively, depending upon the types of chemistry used to construct the left hand side U-V-W-X-Y of compounds of general formula (I), the ketone may require protection e.g. as the dimethyl acetal. Such a method is detailed and exemplified in Scheme 18 by the preparation and use of 3,3-Dimethoxy-hexahydro-pyrrolo[3,2-b]pyrrole-1-carboxylic acid allyl ester (66).

20

-116-



5
Scheme 18. (a) Triethylorthoformate / pTSA / MeOH. (b) Fmoc deprotection, e.g. Solid supported piperidine / DMF (c) Stepwise reaction with intermediates of Y, then X, then W etc., to stepwise construct compounds (68). (d) Alloc deprotection e.g. $(PPh_3)_4Pd^0$ / DCM / $PhSiH_3$ (e) Acylation e.g. $RCOOH$, $tBuOCOC$, NMM, DCM, or SO_2Cl / Pyridine. (f) Trifluoroacetic acid / CH_2Cl_2 / H_2O .

10 The invention extends to novel intermediates as described above, and to processes for preparing compounds of general formula (I) from each of their immediate precursors. In turn, processes for preparing intermediates from their immediate precursors also form part of the invention.

15 Compounds of general formula (I) are useful both as laboratory tools and as therapeutic agents. In the laboratory certain compounds of the invention are useful in establishing whether a known or newly discovered cysteine protease contributes a critical or at least significant biochemical function during the establishment or progression of a disease state, a process commonly referred to as 'target validation'.

20

According to a second aspect of the invention, there is provided a method of validating a known or putative cysteine protease inhibitor as a therapeutic target, the method comprising:

-117-

(a) assessing the *in vitro* binding of a compound as described above to an isolated known or putative cysteine protease, providing a measure of potency; and optionally, one or more of the steps of:

5 (b) assessing the binding of the compound to closely related homologous proteases of the target and general house-keeping proteases (e.g. trypsin) to provides a measure of selectivity;

10 (c) monitoring a cell-based functional marker of a particular cysteine protease activity, in the presence of the compound; and

(d) monitoring an animal model-based functional marker of a particular cysteine protease activity in the presence of the compound.

15 The invention therefore provides a method of validating a known or putative cysteine protease inhibitor as a therapeutic target. Differing approaches and levels of complexity are appropriate to the effective inhibition and 'validation' of a particular target. In the first instance, the method comprises assessing the *in vitro* binding of a compound of general formula (I) to an isolated known or putative
20 cysteine protease, providing a measure of 'potency'. An additional assessment of the binding of a compound of general formula (I) to closely related homologous proteases of the target and general house-keeping proteases (e.g. trypsin) provides a measure of 'selectivity'. A second level of complexity may be assessed by monitoring a cell-based functional marker of a particular cysteine protease
25 activity, in the presence of a compound of general formula (I). For example, a 'human osteoclast resorption assay' has been utilised as a cell-based secondary *in vitro* testing system for monitoring the activity of cathepsin K and the biochemical effect of protease inhibitors (e.g. see WO-A-9850533). An 'MHC-II processing – T-cell activation assay' has been utilised as a cell-based secondary *in vitro* testing
30 system for monitoring the activity of cathepsin S and the biochemical effect of protease inhibitors (Shi, G-P., *et al*, *Immunity*, 10, 197-206, 1999). When investigating viral or bacterial infections such a marker could simply be a

-118-

functional assessment of viral (e.g. count of mRNA copies) or bacterial loading and assessing the biochemical effect of protease inhibitors. A third level of complexity may be assessed by monitoring an animal model-based functional marker of a particular cysteine protease activity, in the presence of a compound of general formula (I). For example, murine models of *Leishmania* infection, *P. vinckei* infection, malaria (inhibition of falcipain) and *T. cruzi* infection (cruzipain), indicate that inhibition of cysteine proteases that play a key role in pathogen propagation is effective in arresting disease symptoms, 'validating' said targets.

10

The invention therefore extends to the use of a compound of general formula (I) in the validation of a known or putative cysteine protease inhibitor as a therapeutic target.

15

Compounds of general formula (I) are useful for the *in vivo* treatment or prevention of diseases in which participation of a cysteine protease is implicated.

20

According to a third aspect of the invention, there is provided a compound of general formula (I) for use in medicine, especially for preventing or treating diseases in which the disease pathology may be modified by inhibiting a cysteine protease.

25

According to a fourth aspect of the invention, there is provided the use of a compound of general formula (I) in the preparation of a medicament for preventing or treating diseases in which the disease pathology may be modified by inhibiting a cysteine protease.

30

Certain cysteine proteases function in the normal physiological process of protein degradation in animals, including humans, e.g. in the degradation of connective tissue. However, elevated levels of these enzymes in the body can result in pathological conditions leading to disease. Thus, cysteine proteases have been implicated in various disease states, including but not limited to, infections by

Pneumocystis carinii, *Trypanosoma cruzi*, *Trypanosoma brucei brucei* and *Crithidia fusiculata*; as well as in osteoporosis, autoimmunity, schistosomiasis, malaria, tumour metastasis, metachromatic leukodystrophy, muscular dystrophy, amyotrophy, and the like. See WO-A-9404172 and EP-A-0603873 and references cited in both of them. Additionally, a secreted bacterial cysteine protease from *S. Aureus* called staphylopain has been implicated as a bacterial virulence factor (Potempa, J., et al. *J. Biol. Chem.*, 262(6), 2664-2667, 1998).

The invention is useful in the prevention and/or treatment of each of the disease states mentioned or implied above. The present invention also is useful in a methods of treatment or prevention of diseases caused by pathological levels of cysteine proteases, particularly cysteine proteases of the papain superfamily, which methods comprise administering to an animal, particularly a mammal, most particularly a human, in need thereof a compound of the present invention. The present invention particularly provides methods for treating diseases in which cysteine proteases are implicated, including infections by *Pneumocystis carinii*, *Trypanosoma cruzi*, *Trypanosoma brucei*, *Leishmania mexicana*, *Clostridium histolyticum*, *Staphylococcus aureus*, foot-and-mouth disease virus and *Crithidia fusiculata*; as well as in osteoporosis, autoimmunity, schistosomiasis, malaria, tumour metastasis, metachromatic leukodystrophy, muscular dystrophy and amyotrophy.

Inhibitors of cathepsin K, particularly cathepsin K-specific compounds, are useful for the treatment of osteoporosis, Paget's disease, gingival diseases such as gingivitis and periodontitis, hypercalcaemia of malignancy, metabolic bone disease, diseases involving matrix or cartilage degradation, in particular osteoarthritis and rheumatoid arthritis and neoplastic diseases.

In accordance with this invention, an effective amount of a compound of general formula (I) may be administered to inhibit the protease implicated with a particular condition or disease. Of course, this dosage amount will further be modified according to the type of administration of the compound. For example,

-120-

to achieve an "effective amount" for acute therapy, parenteral administration of a compound of general formula (I) is preferred. An intravenous infusion of the compound in 5% dextrose in water or normal saline, or a similar formulation with suitable excipients, is most effective, although an intramuscular bolus injection is also useful. Typically, the parenteral dose will be about 0.01 to about 100 mg/kg; preferably between 0.1 and 20 mg/kg, in a manner to maintain the concentration of drug in the plasma at a concentration effective to inhibit a cysteine protease. The compounds may be administered one to four times daily at a level to achieve a total daily dose of about 0.4 to about 400 mg/kg/day. The precise amount of an inventive compound which is therapeutically effective, and the route by which such compound is best administered, is readily determined by one of ordinary skill in the art by comparing the blood level of the agent to the concentration required to have a therapeutic effect. Prodrugs of compounds of the present invention may be prepared by any suitable method. For those compounds in which the prodrug moiety is a ketone functionality, specifically ketals and/or hemiacetals, the conversion may be effected in accordance with conventional methods.

The compounds of this invention may also be administered orally to the patient, in a manner such that the concentration of drug is sufficient to inhibit bone resorption or to achieve any other therapeutic indication as disclosed herein. Typically, a pharmaceutical composition containing the compound is administered at an oral dose of between about 0.1 to about 50 mg/kg in a manner consistent with the condition of the patient. Preferably the oral dose would be about 0.5 to about 20 mg/kg.

No unacceptable toxicological effects are expected when compounds of the present invention are administered in accordance with the present invention. The compounds of this invention, which may have good bioavailability, may be tested in one of several biological assays to determine the concentration of a compound which is required to have a given pharmacological effect.

-121-

According to a fifth aspect of the invention, there is provided a pharmaceutical or veterinary composition comprising one or more compounds of general formula (I) and a pharmaceutically or veterinarily acceptable carrier. Other active materials may also be present, as may be considered appropriate or advisable for the disease or condition being treated or prevented.

The carrier, or, if more than one be present, each of the carriers, must be acceptable in the sense of being compatible with the other ingredients of the formulation and not deleterious to the recipient.

The formulations include those suitable for rectal, nasal, topical (including buccal and sublingual), vaginal or parenteral (including subcutaneous, intramuscular, intravenous and intradermal) administration, but preferably the formulation is an orally administered formulation. The formulations may conveniently be presented in unit dosage form, e.g. tablets and sustained release capsules, and may be prepared by any methods well known in the art of pharmacy.

Such methods include the step of bringing into association the above defined active agent with the carrier. In general, the formulations are prepared by uniformly and intimately bringing into association the active agent with liquid carriers or finely divided solid carriers or both, and then if necessary shaping the product. The invention extends to methods for preparing a pharmaceutical composition comprising bringing a compound of general formula (I) in conjunction or association with a pharmaceutically or veterinarily acceptable carrier or vehicle.

Formulations for oral administration in the present invention may be presented as: discrete units such as capsules, cachets or tablets each containing a predetermined amount of the active agent; as a powder or granules; as a solution or a suspension of the active agent in an aqueous liquid or a non-aqueous liquid; or as an oil-in-water liquid emulsion or a water in oil liquid emulsion; or as a bolus etc.

-122-

For compositions for oral administration (e.g. tablets and capsules), the term "acceptable carrier" includes vehicles such as common excipients e.g. binding agents, for example syrup, acacia, gelatin, sorbitol, tragacanth, polyvinylpyrrolidone (Povidone), methylcellulose, ethylcellulose, sodium carboxymethylcellulose, hydroxypropylmethylcellulose, sucrose and starch; fillers and carriers, for example corn starch, gelatin, lactose, sucrose, microcrystalline cellulose, kaolin, mannitol, dicalcium phosphate, sodium chloride and alginic acid; and lubricants such as magnesium stearate, sodium stearate and other metallic stearates, glycerol stearate stearic acid, silicone fluid, talc waxes, oils and colloidal silica. Flavouring agents such as peppermint, oil of wintergreen, cherry flavouring and the like can also be used. It may be desirable to add a colouring agent to make the dosage form readily identifiable. Tablets may also be coated by methods well known in the art.

A tablet may be made by compression or moulding, optionally with one or more accessory ingredients. Compressed tablets may be prepared by compressing in a suitable machine the active agent in a free flowing form such as a powder or granules, optionally mixed with a binder, lubricant, inert diluent, preservative, surface-active or dispersing agent. Moulded tablets may be made by moulding in a suitable machine a mixture of the powdered compound moistened with an inert liquid diluent. The tablets may be optionally be coated or scored and may be formulated so as to provide slow or controlled release of the active agent.

Other formulations suitable for oral administration include lozenges comprising the active agent in a flavoured base, usually sucrose and acacia or tragacanth; pastilles comprising the active agent in an inert base such as gelatin and glycerin, or sucrose and acacia; and mouthwashes comprising the active agent in a suitable liquid carrier.

Parenteral formulations will generally be sterile.

30

According to a sixth aspect of the invention, there is provided a process for the preparation of a pharmaceutical or veterinary composition as described above, the

-123-

process comprising bringing the active compound(s) into association with the carrier, for example by admixture.

Preferred features for each aspect of the invention are as for each other aspect
5 *mutatis mutandis*.

Experimental Procedures

Solution Phase Chemistry – General Methods

10

15

20

25

30

All solvents were purchased from ROMIL Ltd (Waterbeach, Cambridge, UK) at SpS or Hi-Dry grade unless otherwise stated. General peptide synthesis reagents were obtained from Chem-Impex Intl. Inc. (Wood Dale IL 60191. USA). Thin layer chromatography (TLC) was performed on pre-coated plates (Merck aluminium sheets silica 60 F254, part no. 5554). Visualisation of compounds was achieved under ultraviolet light (254nm) or by using an appropriate staining reagent. Flash column purification was performed on silica gel 60 (Merck 9385). All analytical HPLC were obtained on Phenomenex Jupiter C₄, 5 μ , 300A, 250 x 4.6mm, using mixtures of solvent A = 0.1%aq trifluoroacetic acid (TFA) and solvent B = 90% acetonitrile / 10% solvent A on automated Agilent systems with 215 and / or 254nm UV detection. Unless otherwise stated a gradient of 10 – 90% B in A over 25 minutes at 1.5mL / min was performed for full analytical HPLC analysis. HPLC-MS analysis was performed on an Agilent 1100 series LC/MSD, using automated Agilent HPLC systems, with a gradient of 10 – 90% B in A over 10 minutes on Phenomenex Columbus C₈, 5 μ , 300A, 50 x 2.0mm at 0.4mL / min. Nuclear magnetic resonance (NMR) were obtained on a Bruker DPX400 (400MHz ¹H frequency; QXI probe) in the solvents and temperature indicated. Chemical shifts are expressed in parts per million (δ) and are referenced to residual signals of the solvent. Coupling constants (*J*) are expressed in Hz.

Solid Phase Chemistry – General Methods

Example inhibitors were prepared through a combination of solution and solid phase Fmoc-based chemistries (see 'Solid Phase Peptide Synthesis', Atherton, E. and Sheppard, R. C., IRL Press Ltd, Oxford, UK, 1989, for a general description).
5 An appropriately protected and functionalised building block was prepared in solution (e.g. general compound (6), Scheme 6), then reversibly attached to the solid phase through an appropriate linker. Rounds of coupling / deprotection / chemical modification (Scheme 6). Example inhibitors were then released
10 (cleaved) from the solid phase, analysed, purified and assayed for inhibition verses a range of proteases.

Generally, multipins (polyamide 1.3 → 10µmole loadings, see www.mimotopes.com) were used for the solid phase synthesis, although any suitable solid phase surface could be chosen. In general, the 1.3µmole gears were
15 used to provide small scale crude examples for preliminary screening, whilst the 10µmole crowns were used for scale-up synthesis and purification of preferred examples. Standard coupling and Fmoc deprotection methods were employed (see Grabowska, U. *et al*, *J. Comb. Chem.* 2(5), 475-490, 2000. for a thorough description of solid phase multipin methodologies).

20

Preparation of Initial Assembly

Building Block-linker constructs (e.g.(27), typically 10mg to 100mg) were carboxyl activated with 2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium
25 hexafluoro phosphate (HBTU, 1 mole equivalent), 1-hydroxybenzotriazole.hydrate (HOBT, 1 mole equivalent) and N-methylmorpholine (NMM, 2 mole equivalents) in dimethylformamide (DMF, typically 1 to 10mL) for 5 minutes. Amino functionalised DA/MDA crowns or HEMA gears (10µmole per crown / 1.2µmole per gear, 0.33 mole equivalent of
30 total surface amino functionalisation compared to activated construct) were added, followed by additional DMF to cover the solid phase surface. The loading reaction was left overnight. Following overnight loading, crowns / gears were taken

through standard cycles washing, Fmoc deprotection and loading quantification (see Grabowska, U. *et al*) to provide loaded Building Block-linker constructs (e.g.(28)).

5 Coupling Cycles

The coupling of standard Fmoc-aminoacids (10 or 20 mole equivalent) were performed via carboxyl activated with 2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluoro phosphate (HBTU, 10 or 20mole equivalent), 1-hydroxybenzotriazole.hydrate (HOBT, 10 or 20mole equivalent) and N-methylmorpholine (NMM, 20 or 40mole equivalents) in dimethylformamide, with pre-activation for 5 minutes. Activated species were dispensed to the appropriate wells of a polypropylene 96-well plate (Beckman, 1mL wells, 500µL solution per well for crowns or 250µL solution per well for gears) in a pattern required for synthesis. Loaded free amino Building Block-linker constructs (e.g.(28)) were added and the coupling reaction left overnight. Following overnight coupling, crowns / gears were taken through standard cycles washing and Fmoc deprotection (see Grabowska, U. *et al*). Identical activation and coupling conditions were used for the coupling of a range of carboxylic acids (R-COOH). Alternatively, chloroformates e.g. morpholine-4-carbonylchloride (10mole equivalent), were coupled in DMF with the addition of NMM (10mole equivalents).

Acidolytic Cleavage Cycle

25

A mixture of 95% TFA / 5% water was pre-dispensed into two polystyrene 96-well plates (Beckman, 1mL wells, 600µL solution per well for crowns or 300µL solution per well for gears) in a pattern corresponding to that of the synthesis. The completed multipin assembly was added to the first plate (mother plate), the block covered in tin foil and cleaved for 2 hours. The cleaved multipin assembly was then removed from the first plate and added to the second plate (washing plate)

-126-

for 15 minutes. The spent multipin assembly was then discarded and the mother / washing plates evaporated on an HT-4 GeneVac plate evaporator.

Analysis and Purification of Cleaved Examples

5

(a) Ex 1.2µmole Gears. 100µL dimethylsulphoxide (DMSO) was added to each post cleaved and dried washing plate well, thoroughly mixed, transferred to the corresponding post cleaved and dried mother plate well and again thoroughly mixed. 10µL of this DMSO solution was diluted to 100µL with a 90% acetonitrile / 10% 0.1%aq TFA mixture. 20µL aliquots were analysed by HPLC-MS and full analytical HPLC. In each case the crude example molecules gave the expected $[M + H]^+$ ion and an HPLC peak at > 80% (by 215nm UV analysis). This provided an approximately 10mM DMSO stock solution of good quality crude examples for preliminary protease inhibitory screening.

10

15

(b) Ex 10µmole Crowns. 500µL of a 90% acetonitrile / 10% 0.1%aq TFA mixture was added to each washing plate well, thoroughly mixed, transferred to the corresponding mother plate well and again thoroughly mixed. 5µL of this solution was diluted to 100µL with a 90% acetonitrile / 10% 0.1%aq TFA mixture. 20µL aliquots were analysed by HPLC-MS and full analytical HPLC. In each case the crude example molecules gave the expected $[M + H]^+$ ion and an HPLC peak at > 80% (by 215nm UV analysis). The polystyrene blocks containing crude examples were then lyophilised.

20

(c) Individual examples (ex (b)) were re-dissolved in a 1 : 1 mixture of 0.1% aq TFA / acetonitrile (1mL) and purified by semi-preparative HPLC (Phenomenex Jupiter C₄, 5µ, 300A, 250 x 10mm, a 25-90% B in A gradient over 25mins, 4.0mL/min, 215nm UV detection). Fractions were lyophilised into pre-tarred glass sample vials to provide purified examples (typically 2 to 4mg, 40 to 80% yield).

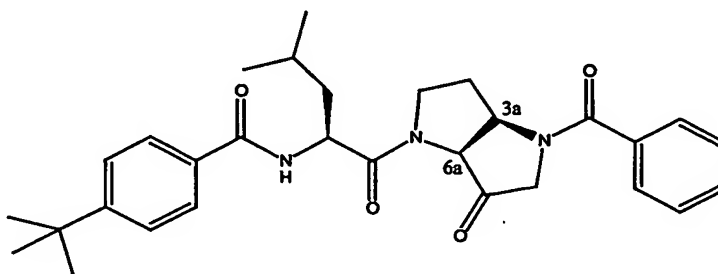
25

(d) Purified examples were dissolved in an appropriate volume of DMSO to provide a 10mM stock solution, for accurate protease inhibitory screening.

30

-127-

EXAMPLE 1. (3*aR*, 6*aS*) · N-[1-(4-Benzoyl-6-oxo-hexahydro-pyrrolo[3,2-b]pyrrole-1-carbonyl)-3-methyl-butyl]-4-tert-butylbenzamide



5

Following the general details from Scheme 1, the required bicycle building block (3*aR*,6*aS*) 3-Oxo-hexahydro-pyrrolo[3,2-b]pyrrole-1,4-dicarboxylic acid 1-tert-butyl ester 4-(9H-fluoren-9-ylmethyl) ester (6) was prepared in 8 steps as follows;

10 (1) Preparation of (2*S*,3*S*) 3-hydroxypyrrolidine-1,2-dicarboxylic acid 1-(9H-fluoren-9-ylmethyl) ester.

Trans-3-hydroxy-L-proline (10.0g, 76.3mmole) was added to a vigorously stirred, ice-cooled solution of sodium carbonate (16.90g, 160.2mmole) in water (100mL). 1,4-Dioxan (75mL) was added providing an opaque but mobile mixture. 9-Fluorenylmethyl chloroformate (20.31g, 80mmole) in 1,4-dioxan (75mL) was added over 1hr, then the ice-cooling removed and the mixture stirred at RT for an additional 2hr. Additional water (300mL) was added, the reaction mixture washed with chloroform (2 x 250mL) and the combined organic layers discarded. The aqueous phase was acidified with 1N HCl to ~ pH 2, providing a thick opaque mixture. The acidified aqueous mixture was extracted with chloroform (2 x 500mL) and the now clear aqueous phase discarded. The opaque combined chloroform layers were dried (Na₂SO₄), filtered and reduced in vacuo to provide batch 1 (5.70g). The residual precipitate (a mixture of product and drying agent) was triturated with hot methanol (2 x 250mL) and the combined methanol solutions reduced in vacuo to provide batch 2 (10.25g). Batch 1 and 2

15

20

25

-128-

were individually analysed by TLC (single UV spot, $R_f = 0.15$, 20% MeOH in CHCl_3), and HPLC-MS (single main UV peak with $R_t = 7.069$ mins, $354.2 [M + H]^+$, $376.2 [M + Na]^+$) and found to be identical, giving a combined yield of 15.95g (45.2mmole, 59.2%). Analysis by ^1H and ^{13}C NMR showed the presence of cis and trans geometrical isomers around the 3° amide bond.

^1H (DMSO- d_6 at 298K); 1.80-2.02 (2H_γ , m), 3.49-3.62 (2H_δ , m), 4.12-4.38 (H_α , H_β , Fmoc H-9 and CH_2 , m), 5.55/5.62 (OH), 7.30-7.31 (2H aromatic, Fmoc H-2 and H-7), 7.35-7.37 (2H aromatic, Fmoc H-3 and H-6), 7.43-7.45 (2H aromatic, Fmoc H-1 and H-8), 7.63-7.65 (2H aromatic, Fmoc H-4 and H-5), 12.8-13.0 (COOH).

^{13}C (DMSO- d_6 at 298K); 31.70/32.70 (d, C_γ), 44.68/45.32 (d, C_δ), 46.94/46.97 (u, Fmoc C-9), 67.04/67.33 (d, Fmoc CH_2), 68.24/68.51 (u, C_α), 73.12/74.23 (u, C_β), 120.49/120.52 (u, Fmoc C-4 and C-5), 125.49/125.58 (u, Fmoc C-1 and C-8), 127.50 (u, Fmoc C-2 and C-7), 128.04 (u, Fmoc C-3 and C-6), 140.99/141.09 (q, Fmoc C-4' and C-5'), 144.02/144.16 (q, Fmoc C-1' and C-8'), 154.33/154.54 (q, OCON), 172.10/172.39 (COOH).

(2) Preparation of (2*S*,3*R*) 3-hydroxypyrrolidine-1,2-dicarboxylic acid 2-allyl ester 1-(9H-fluoren-9-ylmethyl) ester.

(2*S*,3*S*) (3-hydroxy)pyrrolidine-1,2-dicarboxylic acid 1-(9H-fluoren-9-ylmethyl) ester (10.9g, 30.8mmole) was dissolved in toluene (75mL) in a Dean-Stark apparatus. Allyl alcohol (20mL) was added followed by *p*-toluenesulphonic acid.hydrate (6.05g, 31.4mmole). The mixture was refluxed for 1hr, cooled and CHCl_3 (300mL) added. The organic layer was washed with NaHCO_3 (300mL), 0.1N HCl (300mL) and brine (300mL), then dried (Na_2SO_4). Filtration and reduction in vacuo gave a pale yellow foam (13.5g). The crude foam was purified over silica gel (150g) eluting with a gradient of heptane : ethyl acetate 3:1 \rightarrow 1:1. Desired fractions were combined and reduced in vacuo to a colourless gum yield 10.34g

-129-

(26.3mmole, 85.4%). TLC (single UV spot, $R_f = 0.30$, heptane : ethyl acetate 1:1), analytical HPLC $R_t = 18.849$ mins, HPLC-MS (single main UV peak with $R_t = 8.354$ mins, 394.2 $[M + H]^+$, 416.2 $[M + Na]^+$). Analysis by 1H and ^{13}C NMR showed the presence of cis and trans geometrical isomers around the 3° amide bond.

1H ($CDCl_3$ at 298K); 2.00-2.21 ($2H_\gamma$, m), 2.70/2.85 (OH_β , b), 3.72-3.81 ($2H_\delta$, m), 4.12-4.67 (H_α , H_β , Fmoc H-9 and $\underline{CH_2}$, 2 x $COOCH_2CH=CH_2$, m), 5.20-5.40 (2 x $COOCH_2CH=CH_2$, m), 5.82-5.99 (1 x $COOCH_2CH=CH_2$, m), 7.28-7.33 (2H aromatic, Fmoc H-2 and H-7), 7.34-7.41 (2H aromatic, Fmoc H-3 and H-6), 7.53-7.66 (2H aromatic, Fmoc H-1 and H-8), 7.77-7.81 (2H aromatic, Fmoc H-4 and H-5).

^{13}C ($CDCl_3$ at 298K); 32.28/33.04 (d, C_γ), 44.98/45.32 (d, C_δ), 47.56/47.63 (u, Fmoc C-9), 66.44 (d, $COOCH_2CH=CH_2$), 68.01/68.11 (d, Fmoc $\underline{CH_2}$), 68.32/68.72 (u, C_α), 74.49/75.67 (u, C_β), 119.20/119.48 (d, $COOCH_2CH=CH_2$), 120.34/120.37 (u, Fmoc C-4 and C-5), 125.36/125.60 (u, Fmoc C-1 and C-8), 127.47 (u, Fmoc C-2 and C-7), 128.06/128.12 (u, Fmoc C-3 and C-6), 131.79/131.94 (u, $COOCH_2CH=CH_2$), 141.65/141.71 (q, Fmoc C-4' and C-5'), 144.12/144.34 (q, Fmoc C-1' and C-8'), 155.13/155.59 (q, $OCON$), 170.53/170.55 ($\underline{COOCH_2CH=CH_2}$).

(3) Preparation of (2*S*,3*R*) 3-azidopyrrolidine-1,2-dicarboxylic acid 2-allyl ester 1-(9H-fluoren-9-ylmethyl) ester.

Diethyl azodicarboxylate (1.24 ml, 7.9 mmol) was added dropwise over 20 minutes to a stirred solution of triphenylphosphine (2.07 g, 7.9 mmol) in tetrahydrofuran (30 ml) at $0^\circ C$. The mixture was stirred for 5 minutes at $0^\circ C$ then a solution of (2*S*, 3*S*)-3-hydroxypyrrolidine-1,2-dicarboxylic acid 2-allyl ester 1-(9*H*-fluoren-9-ylmethyl) ester (2.59 g, 6.6 mmol) and hydrazoic acid (14.3 ml of 0.7M solution in toluene) in tetrahydrofuran (30 ml) was added dropwise over 35 minutes. The mixture was stirred for 5 minutes at $0^\circ C$ then at ambient temperature for 14 hours. The solvent

-130-

was removed *in vacuo* and the residue purified by flash chromatography over silica gel eluting with a gradient of heptane : ethyl acetate 5:1 \rightarrow 3:1. Appropriate fractions were combined and the solvents removed *in vacuo* to obtain (2*S*, 3*R*) 3-azidopyrrolidine-1,2-dicarboxylic acid allyl ester 1-(9*H*-fluoren-9-ylmethyl) ester as a colourless oil (1.45 g, 53%). TLC (single UV spot, R_f = 0.30, heptane : ethyl acetate 3:1), analytical HPLC main UV peak with R_t = 19.896mins and HPLC-MS 419.2 $[M+H]^+$, 441.2 $[M+Na]^+$.

1H ($CDCl_3$ at 298K); 2.08-2.25 (2H, H-4, m), 3.52-3.59 (1H, H-5, m), 3.68-3.76 (1H, H-5, m), 4.15 (0.5H, Fmoc- $\underline{CH_2}$, t, J = 6.6Hz), 4.24 (0.5H, Fmoc- $\underline{CH_2}$, t, J = 7.1Hz), 4.33-4.38 (2H, H-3 and Fmoc- \underline{CH} , m), 4.44-4.48 (1.5H, 0.5H-2 and Fmoc- \underline{CH} , m), 4.51-4.66 (1.5H, 0.5H-2 and $\underline{CH_2CH=CH_2}$, m), 4.67-4.70 (1H, $\underline{CH_2CH=CH_2}$, m), 5.21-5.40 (2H, $\underline{CH_2CH=CH_2}$, m), 5.84-5.98 (1H, $\underline{CH_2CH=CH_2}$, m), 7.26-7.32 (2H, aromatic, Fmoc H-2 and H-7), 7.37-7.40 (2H, aromatic, Fmoc H-3 and H-6), 7.51-7.60 (2H, aromatic, Fmoc H-1 and H-8), 7.74-7.77 (2H, aromatic, Fmoc H-4 and H-5).

^{13}C ($CDCl_3$ at 298K); 29.14/30.13 (d, C-5), 44.40/44.72 (d, C-5), 47.12/47.21 (u, Fmoc- \underline{CH}), 61.02/61.87 (u, C-3), 61.63/62.07 (u, C-2), 66.17 (d, Fmoc- $\underline{CH_2}$), 67.65 (d, $\underline{CH_2CH=CH_2}$), 118.86/119.11 (d, $\underline{CH_2CH=CH_2}$), 119.94/124.83/124.95/125.05/127.03/127.69 (u, aromatic, Fmoc- \underline{CH}), 131.384/131.50 (u, $\underline{CH_2CH=CH_2}$), 141.29 (q, aromatic Fmoc quaternary carbon b), 143.49/143.65/143.92 (q, aromatic Fmoc quaternary carbon a), 154.07/154.49 (q, Fmoc- \underline{CO}), 168.62/168.70 (q, allyl- \underline{CO}).

(4) Preparation of (2*S*,3*R*) 3-azidopyrrolidine-1,2-dicarboxylic acid 1-(9*H*-fluoren-9-ylmethyl) ester.

Dichloromethane (30 ml) then phenyltrihydrosilane (0.81 ml, 6.6 mmol) were added consecutively to a stirred mixture of tetrakis(triphenylphosphine) palladium(0) (76 mg, 0.066 mmol) and (2*S*,

-131-

3*R*)-3-azidopyrrolidine-1,2-dicarboxylic acid allyl ester 1-(9*H*-fluoren-9-ylmethyl) ester (1.38 g, 3.3 mmol) under argon. The mixture was stirred for 30 minutes then diluted with chloroform (200 ml) and washed with 0.01M hydrochloric acid (200 ml). The aqueous layer was extracted with chloroform (100 ml), then the combined chloroform layers were dried (Na₂SO₄) and the solvent removed *in vacuo*. The brown residue was purified by flash chromatography over silica gel eluting with a gradient of heptane : ethyl acetate 3.5:1 → 0:1 followed by methanol : dichloromethane 1 : 4. Appropriate fractions were combined and the solvents removed *in vacuo* to leave (2*S*, 3*R*) 3-azidopyrrolidine-1,2-dicarboxylic acid 1-(9*H*-fluoren-9-ylmethyl) ester as a brown foam (890 mg, 71%). TLC (main UV spot, R_f = 0.20, methanol : chloroform 1:9), analytical HPLC main UV peak with R_t = 16.528mins and HPLC-MS 379.2 [M+H]⁺, 401.1 [M+Na]⁺, 779.3 [2M+Na]⁺.

(5) Preparation of (2*S*,3*R*) 3-aminopyrrolidine-1,2-dicarboxylic acid 1-(9*H*-fluoren-9-ylmethyl) ester.

Acetic acid was added to a suspension of (2*S*, 3*R*) 3-azidopyrrolidine-1,2-dicarboxylic acid 1-(9*H*-fluoren-9-ylmethyl) ester (3.25 g, 8.6 mmol), palladium on carbon (10%, 320 mg) and ethanol (80 ml) under an atmosphere of argon. The mixture was then stirred under an atmosphere of hydrogen for 3.5 hours then the hydrogen was replaced with argon and the suspension stored at 0°C for 14 hours. A further portion of palladium on carbon (10%, 150 mg) was added then the mixture stirred at ambient temperature for 3 hours under an atmosphere of hydrogen. The catalyst was removed by filtration *in vacuo* through a pad of celite which was washed with acetic acid : water (1:1, 150 ml). The filtrate was concentrated *in vacuo* then toluene (50 ml) was added to the residue and solvents removed *in vacuo*. A further portion of toluene was added (50 ml) and the solvent removed *in vacuo* to leave an oily residue which was triturated with diethyl ether (125 ml) to obtain (2*S*, 3*R*) 3-

-132-

aminopyrrolidine-1,2-dicarboxylic acid 1-(9H-fluoren-9-ylmethyl) ester acetate as a pale brown solid (1.05 g, 30%). Analytical HPLC single UV peak with $R_t = 12.541$ mins and HPLC-MS 353.2 $[M+H]^+$, 705.3 $[2M+Na]^+$.

5

(6) Preparation of (2*S*,3*R*) 3-*tert*-Butoxycarbonylamino-pyrrolidine-1,2-dicarboxylic acid 1-(9H-fluoren-9-ylmethyl) ester

10

15

20

25

A solution of di-*tert*-butyl dicarbonate (210 mg, 0.96 mmol) in 1,4-dioxan (10 ml) was added to a stirred suspension of (2*S*, 3*R*)-3-aminopyrrolidine-1,2-dicarboxylic acid 1-(9H-fluoren-9-ylmethyl) ester (360 mg, 0.87 mmol) and sodium carbonate (195 mg, 1.84 mmol) in water (10 ml) and 1,4-dioxan (10 ml) over 1 hour at 0°C. The reaction mixture was stirred for 16 hours at ambient temperature then the majority of solvents were removed *in vacuo*. The residue was dissolved in dichloromethane (200 ml) and water (100 ml) then acidified to pH ~ 2.5 using 1M hydrochloric acid. The dichloromethane layer was separated then the aqueous layer extracted with dichloromethane. The combined dichloromethane layers were dried (Na_2SO_4) and the solvent removed *in vacuo*. The orange-brown residue was purified by flash chromatography over silica gel eluting with a gradient of dichloromethane : methanol 19:1 → 9:1. Appropriate fractions were combined and the solvents removed *in vacuo* to leave (2*S*, 3*R*) 3-*tert*-butoxycarbonylamino-pyrrolidine-1,2-dicarboxylic acid 1-(9H-fluoren-9-ylmethyl) ester as a light brown solid (235 mg, 60%). TLC (single UV spot, $R_f = 0.25$, methanol : chloroform 1:9), analytical HPLC single UV peak with $R_t = 17.476$ mins and HPLC-MS 397.2 $[M-Bu+2H]^+$, 475.2 $[M+Na]^+$, 927.4 $[2M+Na]^+$.

30

1H ($CDCl_3$ at 298K); 1.35 (2H, brs Me_3C), 1.48 (1H, brs Me_3C), 1.75-2.20 (2H, m, H-4), 2.75-3.85 (4H, m, H-5, H-3, Fmoc-CH), 3.85-4.60 (4H, m, Fmoc-CH₂, H-2 and NH), 6.20-6.75 (0.5H, brs, NH), 7.05-7.90 (8H, aromatic).

δ H (D6-DMSO at 298K); 1.39 and 1.46 (9H total, each s, Me_3C), 1.70-1.85 (1H, m, H-4), 1.70-1.85 (1H, m, H-4), 3.24-3.35 (1H, m, H-5), 3.44-3.54 (1H, m, H-5), 4.02-4.30 (5H, m, H-2, H-3, Fmoc- CH_2 and Fmoc- CH), 6.80 and 7.0 (1H total, each brs, NH), 7.30-7.98 (8H, aromatic)

(7) Preparation of (2*S*,3*R*) 3-*tert*-butoxycarbonylamino-2-(2-diazoacetyl)-pyrrolidine-1,2-dicarboxylic acid 1-carboxylic acid-9*H*-fluoren-9-ylmethyl ester.

A solution of *iso*-butyl chloroformate (68 μl , 0.52 mmol) in dichloromethane (2 ml) and a solution of 4-methylmorpholine (105 μl , 0.95 mmol) in dichloromethane (2 ml) were simultaneously added in portions to a stirred suspension of (2*S*, 3*R*)-3-*tert*-butoxycarbonylamino-2-(2-diazoacetyl)-pyrrolidine-1,2-dicarboxylic acid 1-(9*H*-fluoren-9-ylmethyl) ester (215 mg, 0.48mmol) in dichloromethane (5 ml) at -15 °C over 20 minutes under an atmosphere of nitrogen. The solution was stirred for 2 hours then additional solutions of *iso*-butyl chloroformate (15 μl , 0.115 mmol) in dichloromethane (0.5 ml) and 4-methylmorpholine (26 μl , 0.237 mmol) in dichloromethane (0.5 ml) were simultaneously added in one portion. The mixture was stirred for 30 minutes at -15 °C then ethereal diazomethane [\sim 15mmol generated from diazald (4.7 g mmol) addition in diethyl ether (75 ml) to sodium hydroxide (5.25 g) in water (7.5 ml)/ethanol (15 ml) at 65°C] was cautiously added and the resulting yellow solution stirred at room temperature for 16 hrs. Acetic acid (\sim 1 ml) was cautiously added (until effervescence had ceased), then the mixture was diluted with diethyl ether (100 ml). The ethereal layer was washed with water (3 x 100 ml), dried (Na_2SO_4) and the solvents removed *in vacuo* to leave an oily residue (250 mg) which was purified by flash chromatography over silica gel eluting with a gradient of heptane : ethyl acetate 2:1 \rightarrow 1:1. Appropriate fractions were combined and the solvents removed *in vacuo* to leave (2*S*, 3*R*) 3-*tert*-butoxycarbonylamino-2-(2-

-134-

diazoacetyl)pyrrolidine-1-carboxylic acid 9*H*-fluoren-9-ylmethyl ester as a pale yellow solid (91 mg, 40%). TLC (single UV spot, $R_f = 0.4$, heptane : ethyl acetate 1:1), analytical HPLC main UV peak with $R_t = 18.363$ mins and HPLC-MS 449.2 $[M-N_2+H]^+$, 499.2 $[M+Na]^+$, 975.5 $[2M+Na]^+$.

5

- (8) Cyclisation to (3*aR*,6*aS*) 3-Oxo-hexahydro-pyrrolo[3,2-*b*]pyrrole-1,4-dicarboxylic acid 1-*tert*-butyl ester 4-(9*H*-fluoren-9-ylmethyl) ester (6)

10

A solution of (2*S*, 3*R*) 3-*tert*-butoxycarbonylamino-2-(2-diazoacetyl)pyrrolidine-1-carboxylic acid 9*H*-fluoren-9-ylmethyl ester (100 mg, 0.21 mmol) in chloroform (2.5 ml) was added dropwise over 28 minutes to a stirred suspension of rhodium (II) acetate dimer (10 mg) in toluene (2.5 ml) at 75°C under an atmosphere of argon. The mixture was stirred for an additional 30 minutes at this temperature then the solvents removed *in vacuo* to leave an oily residue which was purified by flash chromatography over silica gel eluting with a gradient of hexane : ethyl acetate 3:1 → 1:1. Appropriate fractions were combined and the solvents removed *in vacuo* to leave (3*aR*, 6*aS*) 3-oxo-hexahydropyrrolo[3,2-*b*]pyrrole-1,4-dicarboxylic acid 1-*tert*-butyl ester 4-(9*H*-fluoren-9-ylmethyl) ester as a white solid (28 mg, 30%). TLC (two UV spots, major and minor $R_f = 0.30$ and 0.35 respectively, hexane : ethyl acetate 7:3), analytical HPLC broad group of UV peaks with $R_t = 20.043$ -21.472 mins and HPLC-MS 449.2 $[M+H]^+$, 471.2 $[M+Na]^+$, 919.4 $[2M+Na]^+$.

15

20

25

δ H (CDCl₃ at 298K); (Spectrum poorly resolved) 1.46 (9H, s, Me₃C), 1.85-2.35 (2H, m, H-6), 3.2-5.0 (9H, m, 2 x H-2, H-3a, 2 x H-5, H-6a, Fmoc-CH₂, Fmoc-CH), 7.2-7.85 (8H, aromatic).

30

Following the general details from Scheme 6, the required bicycle building block (3*aR*,6*aS*) 3-Oxo-hexahydro-pyrrolo[3,2-*b*]pyrrole-1,4-dicarboxylic acid 1-*tert*-butyl ester 4-(9*H*-fluoren-9-ylmethyl) ester (6) was converted to building block-linker construct (27) as follows:

-135-

A solution of sodium acetate trihydrate (42 mg, 0.311 mmol) in water (0.5 ml) was added to a solution of (3aR, 6aS) 3-oxo-hexahydropyrrolo[3,2-*b*]pyrrole-1,4-dicarboxylic acid 1-*tert*-butyl ester 4-(9*H*-fluoren-9-ylmethyl) ester (18.6 mg, 0.0415 mmol) and 4-[[[(hydrazinocarbonyl)amino]methyl]cyclohexane carboxylic acid. trifluoroacetate (Murphy, A. M., *et al*, J. Am. Chem. Soc, 114, 3156-3157, 1992) (68 mg, 0.208 mmol) in ethanol (2.0 ml). Remaining traces of sodium acetate were rinsed into the mixture using a further aliquot of ethanol (1.5 ml) then the reaction heated at 75 °C in a sealed tube for 1 hour. The mixture was stood at ambient temperature for 14 hours then heated at 75 °C for 2.5 hours. The product was extracted into chloroform (60 ml) then washed with hydrochloric acid (0.1M, 2 x 30 ml), saturated aqueous sodium chloride solution (30 ml) then dried (Na₂SO₄) and the solvent removed *in vacuo* to leave the product as a pale yellow oil (22.9 mg, 86%). Analytical HPLC has main UV peaks with Rt = 19.706 and 21.287mins and HPLC-MS (main UV peaks each with 646.3 [M+H]⁺).

Following the general details from Scheme 6, the required building block-linker construct (27) was attached to the solid phase providing loaded building block-linker construct (28) as follows:

Building block-linker construct (27) (35.5µmoles mmoles), 2-(1*H*-benzotriazole-1-yl)-1,1,3,3-tetramethyluroniumhexafluoro phosphate (HBTU, 13.5mg, 35.5µmoles mmoles), 1-hydroxybenzotriazole.hydrate and (HOBT, 5.5mg, 35.5µmoles mmoles) were dissolved in dimethylformamide (1.5mL) and N-methylmorpholine (NMM, 7.8µL, 71µmoles mmoles) added. After pre-activation for 5 minutes, free amine gears (10 x 1.3µmole) were added and left overnight. The spent coupling solution was then added to free amine gears (6 x 1.3µmole) and left overnight. Standard washing and analyses indicated quantitative loading.

Following the general details from Scheme 6, the required loaded building block-linker construct (28) was elaborated on the solid phase as follows:

-136-

Loaded construct (28) was elaborated to EXAMPLE 1 (3*aR*, 6*aS*) N-[1-(4-Benzoyl-6-oxo-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl)-3-methyl-butyl]-4-tert-butylbenz amide by standard Fmoc deprotection and sequential coupling with the appropriate reagents as follows:-

- (i) Fmoc-Leu-OH (2 x 20eq, overnight and 4 hr), HBTU, HOBT, NMM activation in DMF
- (ii) Standard Fmoc deprotection
- 10 (iii) 4-tert-butylbenzoic acid (1 x 10eq, overnight and 4 hr), HBTU, HOBT, NMM activation in DMF
- (iv) Treatment with 50%TFA in dichloromethane for 30mins, followed by washing with 2 x DMF, 1 x 2%NMM in DMF, 1 x DMF, 4 x acetonitrile.
- 15 (v) Benzoic anhydride (20eq) and NMM (5eq) in DMF for 2hr.

The crude example was cleaved and analysed (see general techniques). HPLC Rt = 18.879-19.62mins (>90%), HPLC-MS 504.3 [M + H]⁺, 526.3 [M + Na]⁺.

20 The solid phase experimental detailed for Example 1 may be followed to couple with a vast range of aminoacids, carboxylic acids, sulphonyl chlorides etc to provide a vast range of analogues of general formula I.

25 Alternatively, building blocks may be prepared for solution phase syntheses for example 3-Oxo-hexahydro-pyrrolo[3,2-*b*]pyrrole-1,4-dicarboxylic acid 1-benzyl ester 4-tert-butyl ester (analogue of compound 53, Scheme 15), prepared in 7 steps as follows:

- (1) Preparation of (2*S*, 3*S*) 3-Hydroxypyrrolidine-1,2-dicarboxylic acid 1-tert-butyl ester.
- 30

-137-

Boc anhydride (2.95 g, 13.5 mmol) was added to a stirred solution of the (2*S*, 3*S*)-3-hydroxypyrrolidine-2-carboxylic acid (1.61 g, 12.3 mmol) and sodium carbonate (1.3 g, 12.3 mmol) in a mixture of dioxane (25 ml) and water (12.3 ml). The mixture was stirred for 1.5 h at ambient temperature then evaporated under reduced pressure to afford a residue (~10 ml). The residue was diluted with water (30 ml) then extracted with ethyl acetate (40 ml). The aqueous phase was acidified (pH ~ 2.5) with dilute aqueous hydrochloric acid (0.1 M) then extracted with chloroform (4 x 50 ml). The combined organic layers were dried (Na₂SO₄) and evaporated under reduced pressure to afford (2*S*, 3*S*)-3-hydroxypyrrolidine-1,2-dicarboxylic acid 1-*tert*-butyl ester as a white crystalline solid (2.39 g, ~85%), HPLC-MS (single main peak, 254.1 [M + Na]⁺ and 485.2 [M + H]⁺).

(2) Preparation of (2*S*, 3*S*) 3-Hydroxypyrrolidine-1,2-dicarboxylic acid 2-allyl ester 1-*tert*-butyl ester

A solution of allyl bromide (26 ml, 301 mmol) and tricaprylmethylammonium chloride (38.4 ml, 86.1 mmol) in dichloromethane (307 ml) was added to a stirred solution of (2*S*, 3*S*) 3-hydroxypyrrolidine-1,2-dicarboxylic acid 1-*tert*-butyl ester (19.89 g, 86.1 mmol) and sodium hydrogen carbonate (7.23 g, 86.1 mmol) in water (307 ml). The biphasic mixture was vigorously stirred overnight then diluted with water (100 ml) and the product extracted into dichloromethane (3 x 200 ml). The combined organic layers were dried (Na₂SO₄) and evaporated under reduced pressure to afford a residue. Flash chromatography of the residue over silica gel (400 g) using ethyl acetate : heptane (1 : 4) as the eluent afforded (2*S*, 3*S*) 3-hydroxypyrrolidine-1,2-dicarboxylic acid 2-allyl ester 1-*tert*-butyl ester (9.4 g, 40 %), TLC (single spot, *R*_f = 0.28, 50% ethyl acetate in heptane), HPLC-MS (single main peak, 294.1 [M + Na]⁺, 565.3 [2M + Na]⁺).

-138-

δ_H (400 MHz, $CDCl_3$) 1.41 and 1.46 (combined integration 9H, 2 x s, $C(CH_3)_3$ of geometric isomers), 1.87-1.97 (1H, m, 4-H), 2.06-2.18 (1H, m, 4-H), 2.28-2.36 (1H, m, OH), 3.55-3.71 (2H, m, 5-H₂), 4.20 and 4.32 (combined integration of 1H, 2 x s, 2-H geometric isomers), 4.46 (1H, br. s, 3-H), 4.57-4.73 (1H, m, OCH_2), 5.25-5.37 (2H, m, OCH_2CHCH_2) and 5.86-5.98 (1H, m, OCH_2CHCH_2); δ_C (100 MHz, $CDCl_3$) 28.6 and 28.7 ($C(CH_3)_3$), 32.5 and 32.95 (C-4), 44.5 and 44.9 (C-5), 66.2 (OCH_2), 68.3 (C-2), 74.6 and 75.7 (C-3), 80.6 ($OC(CH_3)_3$), 118.95 and 119.4 (OCH_2CHCH_2), 131.9 (OCH_2CHCH_2), 154.25 and 154.9 (NCO_2), 170.8 and 171.1 (CO_2 Allyl).

(3) Preparation of (2*S*,3*R*) 3-Azido-pyrrolidine-1,2-dicarboxylic acid 2-allyl ester 1-tert-butyl ester

Diethyl azodicarboxylate (0.62 ml, 4.0 mmol) was added dropwise over 25 minutes to a stirred solution of (2*S*, 3*S*) 3-hydroxypyrrolidine-1,2-dicarboxylic acid 2-allyl ester 1-tert-butyl ester (895 mg, 3.3 mmol) and triphenylphosphine (1.08 g, 4.1 mmol) in tetrahydrofuran (30 ml) at 0°C under an atmosphere of argon. The solution was stirred for 5 minutes then diphenylphosphoryl azide (0.89 ml, 4.1 mmol) was added dropwise over 10 minutes. The mixture was stirred for 10 minutes at 0°C then for 24 hours at ambient temperature before removing solvents *in vacuo* to obtain a residue which was purified by flash chromatography over silica gel eluting with a gradient of heptane : ethyl acetate 3:1 → 1:1. Appropriate fractions were combined and the solvents removed *in vacuo* to obtain (2*S*, 3*R*) 3-azidopyrrolidine-1,2-dicarboxylic acid 2-allyl ester 1-tert-butyl ester as a colourless oil (850 mg, 88%) which was contaminated with ~5% of 4,5-dihydropyrrole-1,2-dicarboxylic acid 2-allyl ester 1-tert-butyl ester. TLC (main spot, R_f = 0.70, heptane : ethyl acetate 1:1), HPLC-MS 197.1 $[M-Boc+H]^+$, 241.1 $[M-Bu+2H]^+$, 319.2 $[M+Na]^+$, 615.3 $[2M+Na]^+$.

-139-

^1H (CDCl_3 at 298K); (Doubling up of peaks in spectrum due to restricted rotation around Fmoc amide bond) 1.45 and 1.49 (1.8 and 1.2H respectively, Me_3C , each s), 2.10-2.24 (2H, H-4, m), 3.44-3.52 and 3.60-3.73 (each 1H, H-5, m), 4.31-4.40 (1H, H-3, m), 4.45 and 4.54 (0.6 and 0.4H respectively, H-2, each d, $J = 7.6\text{Hz}$), 4.66-4.78 (2H, $\text{CH}_2\text{CH}=\text{CH}_2$, m), 5.28-5.33 (1H, $\text{CH}_2\text{CH}=\text{CH}_2$, m), 5.42 (1H, $\text{CH}_2\text{CH}=\text{CH}_2$, dd, $J = 17.2$ and 3.7Hz), 5.91-6.04 (1H, $\text{CH}_2\text{CH}=\text{CH}_2$).

^{13}C (CDCl_3 at 298K); 28.40 (u, Me_3C), 29.40/30.18 (d, C-4), 44.22/44.62 (d, C-5), 61.21/61.86/61.98/62.23 (u, C-2 and C-3), 65.81/66.10 (d, $\text{CH}_2\text{CH}=\text{CH}_2$), 80.76/81.24 (q, Me_3C), 118.79/119.21 (d, $\text{CH}_2\text{CH}=\text{CH}_2$), 131.82/131.87 (u, $\text{CH}_2\text{CH}=\text{CH}_2$), 153.53/154.11 (q, OCON), 169.19/169.38 (q, CO_2CH_2).

(4) Preparation of (2*S*, 3*R*) 3-Benzoyloxycarbonylaminopyrrolidine-1,2-dicarboxylic acid 1-*tert*-butyl ester 2-propyl ester

Palladium (10 wt. % on carbon powder, 300 mg) was added portion wise to a solution of (2*S*, 3*R*) 3-azidopyrrolidine-1,2-dicarboxylic acid 2-allyl ester 1-*tert*-butyl ester (790 mg, 2.66 mmol) in ethanol (20 ml) at 0 °C. The mixture was stirred for 2 h under an atmosphere of hydrogen at ambient temperature, then filtered over celite and concentrated *in vacuo* to afford a residue (540 mg). The residue was suspended in dioxane (6 ml) then a solution of sodium carbonate (529 mg, 5 mmol) in water (12 ml) added. The mixture was cooled to 0 °C then a solution of benzyloxy chloroformate (0.314 ml) in dioxane (6 ml) added portion wise over 40 min at 0 °C. The mixture was stirred for 30 min at 0 °C then at ambient temperature for 40 min. Water (150 ml) was added and the products extracted with chloroform (3 x 100 ml), dried (Na_2SO_4) and evaporated under reduced pressure to afford a residue. Flash chromatography of the residue over silica (100 g) using ethyl acetate : heptane (1 : 4) as the eluent

-140-

afforded (2*S*, 3*R*) 3-benzyl oxycarbonylaminopyrrolidine-1,2-dicarboxylic acid 1-*tert*-butyl ester 2-propyl ester (240 mg, 22 %), TLC (single spot, R_f = 0.47, 50% ethyl acetate in heptane); analytical HPLC R_t = 18.06 min, HPLC-MS (single main peak, 429.2 $[M + Na]^+$, 835.4 $[2M + Na]^+$).

5

δ_H (400 MHz, $CDCl_3$) 0.90 (3H, t, J = 7.3 Hz, CH_3), 1.41 and 1.45 (combined integration 9H, 2 x s, $C(CH_3)_3$ of geometric isomers), 1.46-1.66 ($OCH_2CH_2CH_3$), 1.89-2.00 (1H, m, 4- H_2), 2.12-2.25 (1H, m, 4- H_2), 3.32-3.46 (1H, m, 5-H), 3.55-3.72 (1H, m, 5-H), 3.99-4.07 (1H, m, 3-H), 4.46-4.55 ($OCH_2CH_2CH_3$), 4.88-5.17 (combined integration of 3H, m, 2-H and OCH_2Ph), and 7.29-7.42 (6H, m, C_6H_5 and NH); δ_C (100 MHz, $CDCl_3$) 10.5 (CH_3), 22.10 (OCH_2CH_2), 28.41 and 28.50 ($C(CH_3)_3$), 29.4 and 30.5 (C-4), 43.9 and 44.3 (C-5), 52.8 (C-3), 60.5 and 61.3 (C-2), 66.9, 67.0 and 67.2 (OCH_2Ph and OCH_2), 80.5 ($OC(CH_3)_3$), 128.3, 128.4 and 128.7 (*o*-, *m*- and *p*- C_6H_5), 136.2 ($NHCOOCH_2C$), 153.8 and 155.7 (NCO_2 and $NHCO_2$) and 171.1 ($CO_2Propyl$).

10

15

(5) Preparation of (2*S*, 3*R*) 3-Benzyloxycarbonylaminopyrrolidine-1,2-dicarboxylic acid 1-*tert*-butyl ester

20

25

30

A solution of sodium hydroxide (185 mg, 4.6 mmol) in water (1.6 ml) was added to a solution of (2*S*, 3*R*) 3-benzyloxycarbonylaminopyrrolidine-1,2-dicarboxylic acid 1-*tert*-butyl ester 2-propyl ester (229 mg, 0.56 mmol) in ethanol (6 ml). The mixture was stirred for 8 h at ambient temperature. Water (50 ml) was added and the ethanol removed under reduced pressure. The aqueous residue was acidified to pH = 2 by the addition of dilute aqueous hydrochloric acid (0.1 M). The mixture was then extracted with ethyl acetate (3 x 50 ml), dried (Na_2SO_4) and evaporated under reduced pressure to afford (2*S*, 3*R*) 3-benzyloxycarbonylaminopyrrolidine-1,2-dicarboxylic acid 1-*tert*-butyl ester (200 mg, 98%), analytical HPLC R_t = 14.03 min, HPLC-MS (single main peak, 387.2 $[M + Na]^+$, 751.4 $[2M + Na]^+$).

-141-

δ_H (400 MHz, $CDCl_3$) 1.35 and 1.37 (combined integration 9H, 2 x s, $C(CH_3)_3$ of geometric isomers), 1.86-2.15 (2H, m, 4-H₂), 3.14-3.71 (2H, m, 5-H₂), 4.20-4.49 (2H, m, 2-H and 3-H), 5.02-5.22 (2H, m, OCH_2Ph), and 7.18-7.37 (6H, m, C_6H_5 and NH); δ_C (100 MHz, $CDCl_3$) 28.3, 28.4, 28.5 and 29.2 ($C(CH_3)_3$ and C-4), 43.8 and 44.3 (C-5), 52.3 and 53.1 (C-3), 61.0 and 61.4 (C-2), 67.2 and 68.4 (OCH_2Ph), 80.6 and 80.8 ($OC(CH_3)_3$), 128.2, 128.5 and 128.6 and 128.7 (*o*-, *m*- and *p*- C_6H_5), 135.5 ($NHCOOCH_2C$), 153.8 and 154.3 (NCO_2), 158.6 ($NHCO_2$), 175.6 and 175.9 (CO_2H).

(6) Preparation of (2*S*, 3*R*) 3-Benzylloxycarbonylamino-2-(2-diazoacetyl)pyrrolidine-1-carboxylic acid *tert*-butyl ester

(2*S*, 3*R*) 3-benzylloxycarbonylaminopyrrolidine-1,2-dicarboxylic acid 1-*tert*-butyl ester (161 mg, 0.443 mmol) was dissolved with stirring in anhydrous dichloromethane (18 ml). The reaction was flushed with nitrogen and cooled to -15 °C. *iso*-Butylchloroformate (0.063 ml, 0.487 mmol) in anhydrous dichloromethane (1.5 ml) and *N*-methylmorpholine (0.097 ml, 0.886 mmol) in anhydrous dichloromethane (1.5 ml) were added simultaneously in 0.5 ml aliquots over 15 min. The mixture was stirred for 45 min at -15 °C then ethereal diazomethane [generated from addition of diazald (4.7 g, ~15 mmol) in diethyl ether (75 ml) onto sodium hydroxide (5.25 g) in water (7.5 ml) / ethanol (15 ml) at 60 °C] was added to the activated amino acid solution. The mixture was allowed to warm to ambient temperature and stirred for 24 h. A few drops of acetic acid were added to the mixture, followed by diethyl ether (200 ml). The ethereal layer was washed with saturated aqueous sodium hydrogen carbonate (80 ml), dried (Na_2SO_4) and the solvents removed under reduced pressure to give a yellow residue (300 mg). Flash chromatography of the residue over silica (35 g) using ethyl acetate : heptane (1 : 3) afforded (2*S*, 3*R*) 3-benzylloxycarbonylamino-2-(2-diazoacetyl)pyrrolidine-1-carboxylic acid

-142-

tert-butyl ester (150 mg, 87%), TLC (single spot, $R_f = 0.29$, 50% ethyl acetate in heptane); analytical HPLC $R_t = 15.15$ min, HPLC-MS (single main peak, 411.2 $[M + Na]^+$, 799.4 $[2M + Na]^+$).

5 (7) Preparation of (2*S*, 3*R*) 3-Oxohexahydropyrrolo[3,2-*b*]pyrrole-1,4-dicarboxylic acid 1-benzyl ester 4-*tert*-butyl ester

10 A solution of (2*S*, 3*R*) 3-benzyloxycarbonylamino-2-(2-diazoacetyl) pyrrolidine-1-carboxylic acid *tert*-butyl ester (90 mg, 0.23 mmol) was added over 1 h to a refluxing solution of rhodium(II) acetate dimer (2 mg, 0.0046 mmol) in dichloromethane (3 ml). The mixture was heated under reflux for 2 h and the solvent then removed *in vacuo*. The residue was diluted with tetrahydrofuran (40 ml) then filtered through a pad of celite. The filtrate was then concentrated *in vacuo* to afford a residue (106 mg).
15 Flash chromatography of the residue over silica (35 g) using ethyl acetate : heptane (1 : 3) afforded (2*S*, 3*R*) 3-oxohexahydropyrrolo[3,2-*b*]pyrrole-1,4-dicarboxylic acid 1-benzyl ester 4-*tert*-butyl ester (14 mg, 17 %), TLC (two possible rotameric spots, $R_f = 0.30$ and 0.23, 50% ethyl acetate in heptane), analytical HPLC $R_t = 15.479$ min (~60 %), 16.393 (~10 %),
20 17.197 (~10 %), 18.085 (~10 %) and 21.665 (~10 %); HPLC-MS (4 main peaks, 361.0 = $[M + H]^+$, 379 = $[M + H_3O]^+$, 401.0 $[M + H_2O + Na]^+$, $[2M + H]^+ = 721.0$, $[2M + Na]^+ = 743.0$, $[2(M + H_2O) + Na]^+ = 779.0$).

25 δ_H (500 MHz, $CDCl_3$) 1.40-1.50 (9H, m, $C(CH_3)_3$), 1.78-1.86 (1H, m, NCH_2CH_2), 2.30-2.47 (1H, m, NCH_2CH_2), 3.90-4.06 (2H, m, NCH_2), 5.05-5.20 (4H, m, OCH_2 , $BocNCHCO$ and $CbzNCH$), 5.44 (1H, d, $J = 2.2$ Hz, $CbzNCH_2$), 5.56 (1H, br. s, $CbzNCH_2$) and 7.30-7.37 (5H, m, C_6H_5);
 δ_C (126 MHz, $CDCl_3$) 27.5 ($C(CH_3)_3$), 29.6 and 32.2 (NCH_2CH_2), 57.7 ($CbzNCH$), 59.1 (NCH_2), 67.0 (OCH_2), 77.2 ($BocNCH$), 83.5 ($OC(CH_3)_3$),
30 110.7 ($CbzNCH_2$), 128.0, 128.2 and 128.5 (*o*-, *m*- and *p*- C_6H_5), 136.1 (OCH_2C of Cbz), 147.6, 151.4 155.7 and 167.1 ($2 \times NCO_2$ and $CbzNCH_2CO$).

-143-

(8) Preparation of (2*S*, 3*R*) 3-Oxohexahydropyrrolo[3,2-*b*]pyrrole-1-carboxylic acid benzyl ester hydrochloride salt (analogue of compound 54).

5

(2*S*, 3*R*) 3-oxohexahydropyrrolo[3,2-*b*]pyrrole-1,4-dicarboxylic acid 1-benzyl ester 4-*tert*-butyl ester (9 mg, 0.025 mmol) was dissolved in 4M HCl in dioxane (1.25 ml) then stirred for 1 h at room temperature. The mixture was concentrated *in vacuo* then toluene (10 ml) added. The mixture was concentrated once again *in vacuo* and the procedure repeated to afford a residue (10 mg, ~100 %), HPLC-MS (single main peak, 261.1 [M + H]⁺ and 279.1 [M + H₃O]⁺).

10

15 EXAMPLE A. Assays for Cysteine Protease Activity

The compounds of this invention may be tested in one of a number of literature based biochemical assays that are designed to elucidate the characteristics of compound inhibition. The data from these types of assays enables compound potency and the rates of reaction to be measured and quantified. This information, either alone or in combination with other information, would allow the amount of compound required to produce a given pharmacological effect to be determined.

20

General materials and methods

25

Unless otherwise stated, all general chemicals and biochemicals were purchased from either the Sigma Chemical Company, Poole, Dorset, U.K. or from Fisher Scientific UK, Loughborough, Leicestershire, U.K. Absorbance assays were carried out in flat-bottomed 96-well plates (Spectra; Greiner Bio-One Ltd., Stonehouse, Gloucestershire, U.K.) using a SpectraMax PLUS384 plate reader (Molecular Devices, Crawley, U.K.). Fluorescence high throughput assays were carried out in either 384-well microtitre plates (Corning Costar 3705 plates, Fisher Scientific) or 96-well 'U' bottomed Microfluor W1 microtitre plates (Thermo

30

Labsystems, Ashford, Middlesex, U.K.). Fluorescence assays were monitored using a SpectraMax Gemini fluorescence plate reader (Molecular Devices). For substrates employing either a 7-amino-4-methylcoumarin (AMC) or a 7-amino-4-trifluoromethylcoumarin (AFC) fluorophore, assays were monitored at an
5 excitation wavelength of 365 nm and an emission wavelength of 450 nm and the fluorescence plate reader calibrated with AMC. For substrates employing a 3-amino-benzoyl (Abz) fluorophore, assays were monitored at an excitation wavelength of 310 nm and an emission wavelength of 445 nm; the fluorescence plate reader calibrated with 3-amino-benzamide (Fluka). Unless otherwise
10 indicated, all the peptidase substrates were purchased from Bachem UK, St. Helens, Merseyside, UK. Substrates utilizing fluorescence resonance energy transfer methodology (*i.e.* FRET-based substrates) were synthesized at Incenta Limited using published methods (Atherton & Sheppard, *Solid Phase Peptide Synthesis*, IRL Press, Oxford, U.K., 1989) and employed Abz (2-aminobenzoyl)
15 as the fluorescence donor and 3-nitro-tyrosine [Tyr(NO₂)] as the fluorescence quencher (Meldal, M. and Breddam, K., *Anal. Biochem.*, 195, 141-147, 1991). Hydroxyethylpiperazine ethanesulfonate (HEPES), tris-hydroxymethyl aminomethane (tris) base, bis-tris-propane and all the biological detergents (*e.g.* CHAPS, zwittergents, *etc.*) were purchased from CN Biosciences UK, Beeston,
20 Nottinghamshire, U.K. Glycerol was purchased from Amersham Pharmacia Biotech, Little Chalfont, Buckinghamshire, U.K. Stock solutions of substrate or inhibitor were made up to 10 mM in 100 % dimethylsulfoxide (DMSO) (Rathburns, Glasgow, U.K.) and diluted as appropriately required. In all cases the DMSO concentration in the assays was maintained at less than 1% (vol./vol.).

25

Assay protocols were based on literature precedent (Table1; Barrett, A.J., Rawlings, N.D. and Woessner, J.F., 1998, *Handbook of Proteolytic Enzymes*, Academic Press, London and references therein) and modified as required to suit local assay protocols. Enzyme was added as required to initiate the reaction and
30 the activity, as judged by the change in fluorescence upon conversion of substrate to product, was monitored over time. All assays were carried out at 25±1°C.

Table 1. *The enzyme assays described herein were carried out according to literature precedents.*

Enzyme	Buffer	Substrate	Reference
Cathepsin B	I	Z-Phe-Arg-AMC	a, b
Cathepsin H	II	Bz-Phe-Val-Arg-AMC	a, b
Cathepsin L	I	Ac-Phe-Arg-AMC	b, c
Cathepsin S	I	Boc-Val-Leu-Lys-AMC	c, d
Caspase 1	III	Ac-Leu-Glu-His-Asp-AMC	e
Caspase 2	III	Z-Val-Asp-Val-Ala-Asp-AFC	f
Caspase 3	III	Ac-Asp-Glu-Val-Asp-AMC	g, h
Caspase 4	III	Suc-Tyr-Val-Ala-Asp-AMC	f
Caspase 5	III	Ac-Leu-Glu-His-Asp-AMC	
Caspase 6	III	Ac-Val-Glu-Ile-Asp-AMC	i, j, k
Caspase 7	III	Ac-Asp-Glu-Val-Asp-AMC	
Caspase 8	III	Ac-Ile-Glu-Thr-Asp-AMC	l
Caspase 9	III	Ac-Leu-Glu-His-Asp-AMC	
Caspase 10	III	Ac-Ile-Glu-Thr-Asp-AMC	
Cruzipain	IV	D-Val-Leu-Lys-AMC	m, n
CPB2.8ΔCTE	XI	Pro-Phe-Arg-AMC	q
<i>S. Aureus</i> Extracellular cysteine peptidase	I	Abz-Ile-Ala-Ala-Pro-Tyr(NO ₂)-Glu-NH ₂	o
Clostripain		Z-Gly-Gly-Arg-AMC	p
FMDV LP	V	Abz-Arg-Lys-Leu-Lys-Gly-Ala-Gly-Ser-Tyr(NO ₂)-Glu-NH ₂	r
Trypsin	VI	Z-Gly-Gly-Arg-AMC	s
Calpain μ	VII	Abz-Ala-Asn-Leu-Gly-Arg-Pro-Ala-Leu-Tyr(NO ₂)-Asp-NH ₂	t
Calpain m	VIII	Abz-Lys-Leu-Cys(Bzl)-Phe-Ser-Lys-Gln-Tyr(NO ₂)-Asp-NH ₂	t

-146-

Cathepsin K	IX	Z-Phe-Arg-AMC	u
Cathepsin X	X		v,w

- I: 10 mM BTP, pH 6.5 containing 1 mM EDTA, 5 mM 2-mercaptoethanol and 1 mM CaCl₂
- 5 II: 10 mM BTP, pH 6.5 containing 1 mM EDTA, 142 mM NaCl, 1 mM DTT, 1 mM CaCl₂, 0.035 mM Zwittergent 3-16
- III: 50mM HEPES pH 7.2, 10% Glycerol, 0.1% CHAPS, 142 mM NaCl, 1 mM EDTA, 5 mM DTT
- IV: 100 mM sodium phosphate, pH 6.75 containing 1 mM EDTA and 10 mM L-cysteine
- 10 V: 50 mM trisacetate, pH 8.4 containing 1 mM EDTA, 10 mM L-cysteine and 0.25% (w/v) CHAPS
- VI: 10 mM HEPES, pH 8.0 containing 5 mM CaCl₂
- VII: 10 mM HEPES, pH 7.5 containing 2 mM 2-mercaptoethanol and 100 µM CaCl₂
- 15 VIII: 10 mM HEPES, pH 7.5 containing 2 mM 2-mercaptoethanol and 200 µM CaCl₂
- IX: 100 mM sodium acetate; pH 5.5 containing 10 mM L-cysteine and 1 mM EDTA
- X: 100 mM sodium acetate; pH 5.5 containing 10 mM L-cysteine; 0.05% (w/v) Brij 35 and 1 mM EDTA
- 20 XI: 100 mM sodium acetate; pH 5.5 containing 10 mM L-cysteine; 142 mM sodium chloride and 1 mM EDTA

^a Barrett, A.J., *Biochem. J.*, 187, 909-912, 1980

25 ^b Barrett, A.J. and Kirschke, H., *Methods Enzymol.*, 80, 535-561, 1981

^c Quibell, M. and Taylor, S., *WO0069855*, 2000

^d Bromme, D., Steinert, ., Freibe, S., Fittkau, S., Wiederanders, B., and Kirschke, H., *Biochem. J.*, 264, 475-481, 1989

^e Rano, T.A., *et. al.*, *Chem. Biol.*, 4, 149, 1997

30 ^f Talanian, R.V., *et. al.*, *J. Biol. Chem.*, 272, 9677, 1997

- ^g Lazebnik, Y.A., Kaufmann, S.H., Desnoyers, S., Poirer, G.G. and Earnshaw, W.C., *Nature.*, 371, 768-774, 1994
- ^h Han, Z., et. al., *J. Biol. Chem.*, 272, 13432, 1997
- ⁱ Takahashi, A., et. al., *PNAS*, 93, 8395, 1996
- 5 ^j Martins, L.M., et. al., *J. Biol. Chem.*, 272, 7421, 1997
- ^k Nagata, S., *Cell.*, 88, 355, 1997
- ^l Harris, J.L., et. al., *J. Biol. Chem.*, 273, 27364, 1998
- ^m Cazzulo, J.J., Cazzulo Franke, M.C., Martinez, J. and Franke de Cazzulo, B.M., *Biochim. Biophys. Acta.*, 1037, 186-191, 1990
- 10 ⁿ Cazzulo, J.J., Bravo, M., Raimondi, A., Engstrom, U., Lindeberg, G. and Hellman, U., *Cell Mol. Biol.*, 42, 691-696, 1996
- ^o Potempa, J., Dubin, A., Korzus, G. and Travis, J., *Biochem. J.*, 263, 2664-2667, 1988
- ^p Kembhavi, A.A., Buttle, D.J., Rauber, P. and Barrett, A.J., *FEBS Lett.*, 283, 277-15 280, 1991
- ^q Alves, L.C., et. al., *Mol. Biochem. Parasitol*, 116, 1-9, 2001.
- ^r Guarné, et.al., *J. Mol. Biol.*, 302, 1227-1240, 2000.
- ^s Halfon and Craik, (Barret, Rawlings and Woessner, eds.), in *Handbook of Proteolytic Enzymes*, Academic Press, London, 12-21, 1998.
- 20 ^t Sasaki, et. al., (1984), *J. Biol. Chem.*, 259, 12489-12494, 1984.
- ^u Bossard, M.J., et. al., , *J. Biol. Chem.*, 271, 12517-12524, 1996
- ^v Santamaria, I., et. al., *J. Biol. Chem.*, 273, 16816-16823, 1998
- ^w Klemencic, J, et al., *Eur.J.Biochem.*, 267, 5404-5412, 2000
- 25 Trypanosoma cruzi cruzipain peptidase activity assays

Wild-type cruzipain, derived from *Trypanosoma cruzi* Dm28 epimastigotes, was obtained from Dr. Julio Scharfstein (Instituto de Biofisica Carlos Chagas Filho, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil). Activity assays

30 were carried out in 100 mM sodium phosphate, pH 6.75 containing 1 mM EDTA and 10 mM L-cysteine using 2.5 nM enzyme. Ac-Phe-Arg-AMC ($K_M^{app} \approx 12 \mu M$) and D-Val-Leu-Lys-AMC ($K_M^{app} \approx 4 \mu M$) were used as the substrates. Routinely,

-148-

Ac-FR-AMC was used at a concentration equivalent to K_M^{app} and D-Val-Leu-Lys-AMC was used at a concentration of 25 μ M. The rate of conversion of substrate to product was derived from the slope of the increase in fluorescence monitored continuously over time.

5

Leishmania mexicana cysteine protease B (CPB) peptidase activity assays

Wild-type recombinant CPB without the C-terminal extension (*i.e.* CPB2.8 Δ CTE; Sanderson, S.J., *et. al.*, *Biochem. J.*, 347, 383-388, 2000) was obtained from Dr. Jeremy Mottram (Wellcome Centre for Molecular Parasitology, The Anderson College, University of Glasgow, Glasgow, U.K.). Activity assays were carried out in 100 mM sodium acetate; pH 5.5 containing 1 mM EDTA; 200 mM NaCl and 10 mM DTT (Alves, L.C., *et. al.*, *Mol. Biochem. Parasitol.*, 116, 1-9, 2001) using 0.25 nM enzyme. Pro-Phe-Arg-AMC ($K_M^{app} \approx 38\mu$ M) was used as the substrate at a concentration equivalent to K_M^{app} . The rate of conversion of substrate to product was derived from the slope of the increase in fluorescence monitored continuously over time.

15

Cathepsin peptidase activity assays

20

Bovine cathepsin S, human cathepsin L, human cathepsin H and human cathepsin B were obtained from CN Biosciences. Recombinant human cathepsin S, human cathepsin K and human cathepsin X were obtained from Dr. Boris Turk (Josef Stefan Institute, Ljubljana, Slovenia). Unless otherwise stated, all peptidase activity assays were carried out in 10 mM bis-tris-propane (BTP), pH 6.5 containing 1 mM EDTA, 5 mM 2-mercaptoethanol and 1 mM CaCl_2 . Human cathepsin H activity assays were carried out in 10 mM BTP pH 6.5, 142 mM NaCl, 1 mM CaCl_2 , 1 mM EDTA, 1 mM DTT, 0.035 mM Zwittergent 3-16. Human cathepsin K assays were carried out in 100 mM sodium acetate; pH 5.5 containing 20 mM L-cysteine and 1 mM EDTA (Bossard, M.J., *et. al.*, *J. Biol. Chem.*, 271, 12517-12524, 1996). Human cathepsin X assays were carried out in 100 mM sodium acetate; pH 5.5 containing 20 mM L-cysteine; 0.05% (w/v) Brij 35 and 1 mM EDTA (Santamaria, I., *et. al.*, *J. Biol. Chem.*, 273, 16816-16823,

25

30

-149-

1998; Klemencic, J, *et al.*, *Eur. J. Biochem.*, 267, 5404-5412, 2000). The final enzyme concentrations used in the assays were 0.5 nM bovine cathepsin S, 1 nM cathepsin L, 0.1 nM cathepsin B, 0.25nM Cathepsin K; 1 nM cathepsin X and 10 nM cathepsin H. For the inhibition assays, the substrates used for cathepsin S, cathepsin L, cathepsin B, cathepsin K and cathepsin H were boc-Val-Leu-Lys-AMC ($K_M^{app} \approx 30 \mu\text{M}$), Ac-Phe-Arg-AMC ($K_M^{app} \approx 20 \mu\text{M}$), Z-Phe-Arg-AMC ($K_M^{app} \approx 40 \mu\text{M}$), Z-Leu-Arg-AMC ($K_M^{app} \approx 2\mu\text{M}$); Bz-Phe-Val-Arg-AMC ($K_M^{app} \approx 150 \mu\text{M}$) respectively. In each case the substrate concentration used in each assay was equivalent to the K_M^{app} . The rate of conversion of substrate to product was derived from the slope of the increase in fluorescence monitored continuously over time.

Trypsin peptidase activity assays

Human pancreatic trypsin (iodination grade; CN Biosciences) activity assays were carried out in 10 mM HEPES, pH 8.0 containing 5 mM CaCl_2 using 0.1 nM trypsin. For the inhibition assays, Z-Gly-Gly-Arg-AMC ($K_M^{app} \approx 84 \mu\text{M}$) was used as the substrate at a concentration equivalent to K_M^{app} . The rate of conversion of substrate to product was derived from the slope of the increase in fluorescence monitored continuously over time.

Clostripain peptidase activity assays

Clostripain (Sigma) activity assays were carried out in 10 mM BTP, pH 6.5 containing 1 mM EDTA, 5 mM 2-mercaptoethanol and 1mM CaCl_2 using 0.3 nM enzyme. For the inhibition assays, Z-Gly-Gly-Arg-AMC ($K_M^{app} \approx 100 \mu\text{M}$) was used as the substrate at a concentration equivalent to K_M^{app} . The rate of conversion of substrate to product was derived from the slope of the increase in fluorescence monitored continuously over time.

Calpain peptidase activity assays

-150-

Calpain (human erythrocyte μ -calpain and porcine kidney m-calpain; CN Biosciences) activity assays were carried out in 10 mM HEPES, pH 7.5 containing 2 mM 2-mercaptoethanol and CaCl_2 using 25 nM of either enzyme (Sasaki, *et. al.*, *J. Biol. Chem.*, **259**, 12489-12494, 1984). For μ -calpain inhibition
5 assays, the buffer contained 100 μM CaCl_2 and Abz-Ala-Asn-Leu-Gly-Arg-Pro-Ala-Leu-Tyr(NO_2)-Asp- NH_2 ($K_M^{\text{app}} \approx 20 \mu\text{M}$; Incenta Limited) was used as the substrate. For m-calpain inhibition assays, the assay buffer contained 200 μM CaCl_2 and Abz-Lys-Leu-Cys(Bzl)-Phe-Ser-Lys-Gln-Tyr(NO_2)-Asp- NH_2 ($K_M^{\text{app}} \approx$
10 22 μM ; Incenta Limited) was used as the substrate. In both cases the substrate concentration employed in the assays was equivalent to the K_M^{app} . The rate of conversion of substrate to product was derived from the slope of the increase in fluorescence monitored continuously over time.

15 Extracellular *S. aureus* V8 cysteine peptidase (staphylopain) peptidase activity assays

S. aureus V8 was obtained from Prof. S. Arvidson, Karolinska Institute, Stockholm, Sweden. Extracellular *S. aureus* V8 cysteine peptidase (staphylopain) activity assays were carried out using partially purified *S. aureus* V8 culture
20 supernatant (obtained from Dr. Peter Lambert, Aston University, Birmingham, U.K.). Activity assays were carried out in 10 mM BTP, pH 6.5 containing 1 mM EDTA, 5 mM 2-mercaptoethanol and 1mM CaCl_2 using two-times diluted partially purified extract. For the inhibition assays, Abz-Ile-Ala-Ala-Pro-Tyr(NO_2)-Glu- NH_2 ($K_M^{\text{app}} \approx 117 \mu\text{M}$; Incenta Limited) was used as the substrate
25 at a concentration equivalent to K_M^{app} . The rate of conversion of substrate to product was derived from the slope of the increase in fluorescence monitored continuously over time.

Foot-and-mouth disease leader peptidase (FMDV-LP) activity assays

30 Recombinant wild-type FMDV-LP was obtained from Dr. Tim Skern (Institut für Medizinische Biochemie, Abteilung für Biochemie, Universität Wien, Wien, Austria). Activity assays were carried out in 50 mM trisacetate, pH 8.4

-151-

containing 1 mM EDTA, 10 mM L-cysteine and 0.25% (w/v) CHAPS using 10 nM enzyme. For the inhibition assays, Abz-Arg-Lys-Leu-Lys-Gly-Ala-Gly-Ser-Tyr(NO₂)-Glu-NH₂ ($K_M^{app} \approx 51 \mu\text{M}$, Incenta Limited) was used as the substrate at a concentration equivalent to K_M^{app} . The rate of conversion of substrate to product was derived from the slope of the increase in fluorescence monitored continuously over time.

Caspase peptidase activity assays

Caspases 1-10 were obtained from CN Biosciences or BioVision Inc. (Mountain View, CA, USA) and all assays were carried out in 50mM HEPES; pH 7.2, 10% (v/v) glycerol, 0.1% (w/v) CHAPS, 142 mM NaCl, 1 mM EDTA, 5 mM dithiothreitol (DTT) using 0.1-1 U per assay. For caspase 1, Ac-Leu-Glu-His-Asp-AMC was used as the substrate; for caspase 2, Z-Val-Asp-Val-Ala-Asp-AFC was used as the substrate; for caspase 3, Ac-Asp-Glu-Val-Asp-AMC was used as the substrate; for caspase 4, Suc-Tyr-Val-Ala-Asp-AMC was used as the substrate; for caspase 5, Ac-Leu-Glu-His-Asp-AMC was used as the substrate; for caspase 6, Ac-Val-Glu-Ile-Asp-AMC was used as the substrate; for caspase 7, Ac-Asp-Glu-Val-Asp-AMC was used as the substrate; for caspase 8, Ac-Ile-Glu-Thr-Asp-AMC was used as the substrate; for caspase 9, Ac-Leu-Glu-His-Asp-AMC was used as the substrate; for caspase 10, Ac-Ile-Glu-Thr-Asp-AMC was used as the substrate (Nicholson, D.W. and Thornberry, N.A., *TIBS*, **22**, 299-306, 1997; Stennicke, H.R. and Salvesen, G.S., *J. Biol. Chem.*, **272**(41), 25719-25723, 1997; Talanian, R.V., *et. al.*, *J. Biol. Chem.*, **272**(15), 9677-9682, 1997; Wolf, B.B. and Green, D.R., *J. Biol. Chem.*, **274**(29), 20049-20052, 1999). The rate of conversion of substrate to product was derived from the slope of the increase in fluorescence monitored continuously over time.

Measurement of the apparent macroscopic binding (Michaelis) constants (K_M^{app}) for substrates

The apparent macroscopic binding constant (K_M^{app}) for each substrate was calculated, from the dependence of enzyme activity as a function of substrate

-152-

concentration. The observed rates were plotted on the ordinate against the related substrate concentration on the abscissa and the data fitted by direct regression analysis (Prism v 3.02; GraphPad, San Diego, USA) using Equation 1 (Cornish-Bowden, A. *Fundamentals of enzyme kinetics* Portland Press; 1995, 93-128.).

5

$$v_i = \frac{V_{\max}^{\text{app}} \cdot [S_o]}{[S_o] + K_M^{\text{app}}} \quad (1)$$

In Equation 1 ' v_i ' is the observed initial rate, ' V_{\max}^{app} ' is the observed maximum activity at saturating substrate concentration, ' K_M^{app} ' is the apparent macroscopic binding (Michaelis) constant for the substrate, ' $[S_o]$ ' is the initial substrate concentration.

10

Measurement of the inhibition constants

The apparent inhibition constant (K_i) for each compound was determined on the basis that inhibition was reversible and occurred by a pure-competitive mechanism. The K_i values were calculated, from the dependence of enzyme activity as a function of inhibitor concentration, by direct regression analysis (Prism v 3.02) using Equation 2 (Cornish-Bowden, A., 1995.).

20

$$v_i = \frac{V_{\max}^{\text{app}} \cdot [S]}{[S] + \{K_M^{\text{app}} \cdot ([I] / K_i)\}} \quad (2)$$

In Equation 2 ' v_i ' is the observed residual activity, ' V_{\max}^{app} ' is the observed maximum activity (i.e. in the absence of inhibitor), ' K_M^{app} ' is the apparent macroscopic binding (Michaelis) constant for the substrate, ' $[S]$ ' is the initial substrate concentration, ' K_i ' is the apparent dissociation constant and ' $[I]$ ' is the inhibitor concentration.

25

In situations where the apparent dissociation constant (K_i^{app}) approached the enzyme concentrations, the K_i^{app} values were calculated using a quadratic solution in the form described by Equation 3 (Morrison, J.F. *Trends Biochem. Sci.*, 7, 102-

30

105, 1982; Morrison, J.F. *Biochim. Biophys. Acta*, 185, 269-286, 1969; Stone, S.R. and Hofsteenge, J. *Biochemistry*, 25, 4622-4628, 1986).

$$v_i = \frac{F\{E_o - I_o - K_i^{app} + \sqrt{(E_o - I_o - K_i^{app})^2 + 4K_i^{app}E_o}\}}{2} \quad (3)$$

5

$$K_i^{app} = K_i(1 + [S_o]/K_M^{app}) \quad (4)$$

In Equation 3 ' v_i ' is the observed residual activity, ' F ' is the difference between the maximum activity (*i.e.* in the absence of inhibitor) and minimum enzyme activity, ' E_o ' is the total enzyme concentration, ' K_i^{app} ' is the apparent dissociation constant and ' I_o ' is the inhibitor concentration. Curves were fitted by non-linear regression analysis (Prism) using a fixed value for the enzyme concentration. Equation 4 was used to account for the substrate kinetics, where ' K_i ' is the inhibition constant, ' $[S_o]$ ' is the initial substrate concentration and ' K_M^{app} ' is the apparent macroscopic binding (Michaelis) constant for the substrate (Morrison, 1982).

The second-order rate of reaction of inhibitor with enzyme

Where applicable, the concentration dependence of the observed rate of reaction (k_{obs}) of each compound with enzyme was analysed by determining the rate of enzyme inactivation under pseudo-first order conditions in the presence of substrate (Morrison, J.F., *TIBS*, 102-105, 1982; Tian, W.X. and Tsou, C.L., *Biochemistry*, 21, 1028-1032, 1982; Morrison, J.F. and Walsh, C.T., from Meister (Ed.), *Advances in Enzymol.*, 61, 201-301, 1988; Tsou, C.L., from Meister (Ed.), *Advances in Enzymol.*, 61, 381-436, 1988;). Assays were carried out by addition of various concentrations of inhibitor to assay buffer containing substrate. Assays were initiated by the addition of enzyme to the reaction mixture and the change in fluorescence monitored over time. During the course of the assay less than 10% of the substrate was consumed.

-154-

$$F = v_s t + \frac{(v_o - v_s)[1 - e^{-(k_{obs}t)}]}{k_{obs}} + D \quad (5)$$

The activity fluorescence progress curves were fitted by non-linear regression analysis (Prism) using Eq. 5 (Morrison, 1969; Morrison, 1982); where 'F' is the fluorescence response, 't' is time, 'v_o' is the initial velocity, 'v_s' is the equilibrium steady-state velocity, 'k_{obs}' is the observed pseudo first-order rate constant and 'D' is the intercept at time zero (*i.e.* the ordinate displacement of the curve). The second order rate constant was obtained from the slope of the line of a plot of k_{obs} versus the inhibitor concentration (*i.e.* k_{obs}/[I]). To correct for substrate kinetics, Eq. 6 was used, where '[S_o]' is the initial substrate concentration and 'K_M^{app}' is the apparent macroscopic binding (Michaelis) constant for the substrate.

$$k_{inact} = \frac{k_{obs}(1 + [S_o]/K_M^{app})}{[I]} \quad (6)$$

15

Compounds of the invention were tested by the above described assays and observed to exhibit cathepsin K inhibitory activity or inhibitory activity against an alternative CA C1 cysteine protease with an *in vitro* K_i inhibitory constant of less than or equal to 100μM. Exemplary inhibition data for Example 1 of the invention are given in table 2.

20

Table 2. Exemplary inhibition data (K_i expressed as μM).

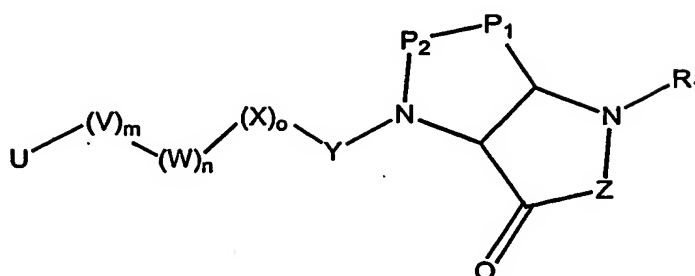
Human Cathepsin K	Cruzipain	Bovine Cathepsin S	Human Cathepsin L	CPB
<0.5	>1	>10	>15	>8

-155-

CLAIMS

1. A compound of general formula (I)

5



(I)

wherein:

10

$Z = CR^3R^4$, where R^3 and R^4 are independently chosen from C_{0-7} -alkyl (when $C = 0$, R^3 or R^4 is simply a hydrogen atom), C_{3-6} -cycloalkyl, Ar- C_{0-7} -alkyl (when $C = 0$, R^3 or R^4 is simply an aromatic moiety Ar),

15

$P_1 = CR^5R^6$, where R^5 and R^6 are independently chosen from C_{0-7} -alkyl, C_{3-6} -cycloalkyl, Ar- C_{0-7} -alkyl, O- C_{0-7} -alkyl, O- C_{3-6} -cycloalkyl, O-Ar- C_{0-7} -alkyl, S- C_{0-7} -alkyl, S- C_{3-6} -cycloalkyl, S-Ar- C_{0-7} -alkyl, NH- C_{0-7} -alkyl, NH- C_{3-6} -cycloalkyl, NH-Ar- C_{0-7} -alkyl, $N(C_{0-7}\text{-alkyl})_2$, $N(C_{3-6}\text{-cycloalkyl})_2$ or $N(\text{Ar-}C_{0-7}\text{-alkyl})_2$;

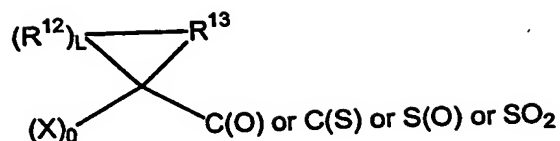
20

$P_2 = O$, CR^7R^8 or NR^9 , where R^7 and R^8 are independently chosen from C_{0-7} -alkyl, C_{3-6} -cycloalkyl, Ar- C_{0-7} -alkyl and R^9 is chosen from C_{0-7} -alkyl, C_{3-6} -cycloalkyl or Ar- C_{0-7} -alkyl;

25

$Y = CR^{10}R^{11}\text{-C(O)}$ or $CR^{10}R^{11}\text{-C(S)}$ or $CR^{10}R^{11}\text{-S(O)}$ or $CR^{10}R^{11}\text{-SO}_2$ where R^{10} and R^{11} are independently chosen from C_{0-7} -alkyl, C_{3-6} -cycloalkyl and Ar- C_{0-7} -alkyl, or Y represents

-156-



5 where L is a number from one to four and R^{12} and R^{13} are independently chosen from $CR^{14}R^{15}$ where R^{14} and R^{15} are independently chosen from C_{0-7} -alkyl, C_{3-6} -cycloalkyl, Ar- C_{0-7} -alkyl or halogen; and for each R^{12} and R^{13} either R^{14} or R^{15} (but not both R^{14} and R^{15}) may additionally be chosen from O- C_{0-7} -alkyl, O- C_{3-6} -cycloalkyl, O-Ar- C_{0-7} -alkyl, S- C_{0-7} -alkyl, S- C_{3-6} -cycloalkyl, S-Ar- C_{0-7} -alkyl, NH- C_{0-7} -alkyl, NH- C_{3-6} -cycloalkyl, NH-Ar- C_{0-7} -alkyl, N-(C_{0-7} -alkyl)₂, N-(C_{3-6} -cycloalkyl)₂, and N-(Ar- C_{0-7} -alkyl)₂;

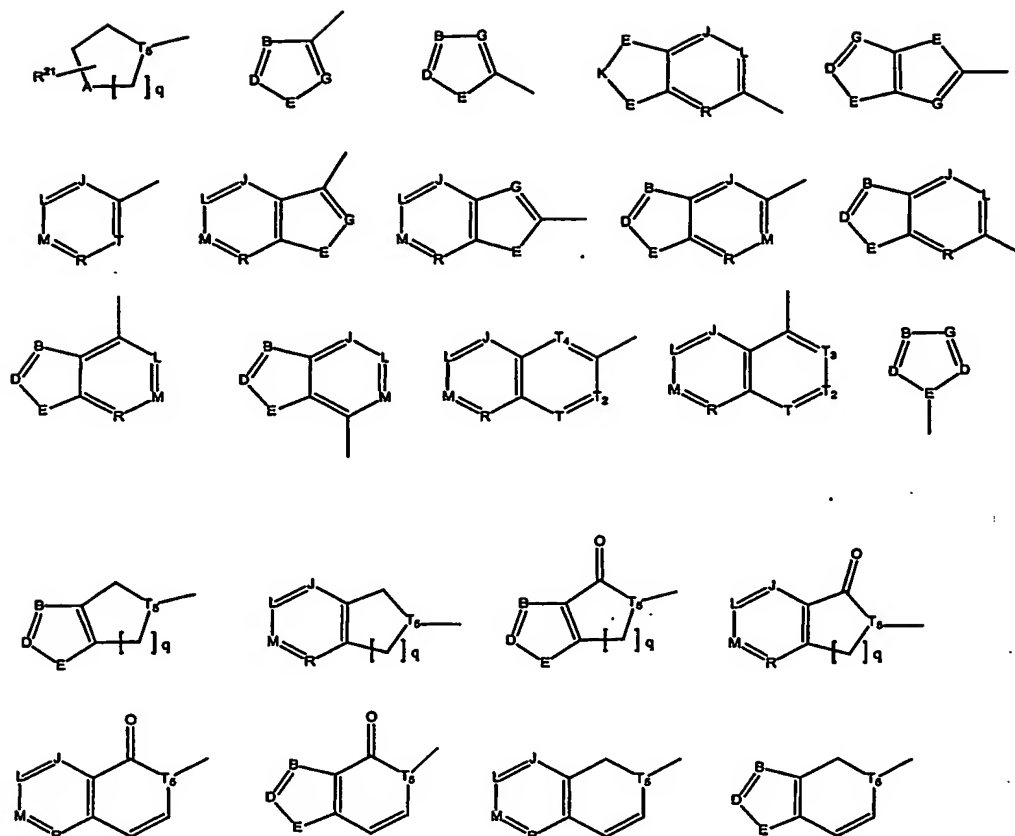
10 $(X)_0 = CR^{16}R^{17}$, where R^{16} and R^{17} are independently chosen from C_{0-7} -alkyl, C_{3-6} -cycloalkyl and Ar- C_{0-7} -alkyl and o is a number from zero to three;

15 $(W)_n = O, S, C(O), S(O) \text{ or } S(O)_2 \text{ or } NR^{18}$, where R^{18} is chosen from C_{0-7} -alkyl, C_{3-6} -cycloalkyl and Ar- C_{0-7} -alkyl and n is zero or one;

20 $(V)_m = C(O), C(S), S(O), S(O)_2, S(O)_2NH, OC(O), NHC(O), NHS(O), NHS(O)_2, OC(O)NH, C(O)NH \text{ or } CR^{19}R^{20}$, where R^{19} and R^{20} are independently chosen from C_{0-7} -alkyl, C_{3-6} -cycloalkyl, Ar- C_{0-7} -alkyl and m is a number from zero to three, provided that when m is greater than one, $(V)_m$ contains a maximum of one carbonyl or sulphonyl group;

25 U = a stable 5- to 7-membered monocyclic or a stable 8- to 11-membered bicyclic ring which is either saturated or unsaturated and which includes zero to four heteroatoms (as detailed below):

-157-



wherein R^{21} is:

- 5 C_{0-7} -alkyl, C_{3-6} -cycloalkyl, Ar- C_{0-7} -alkyl, O- C_{0-7} -alkyl, O- C_{3-6} -cycloalkyl, O-Ar- C_{0-7} -alkyl, S- C_{0-7} -alkyl, S- C_{3-6} -cycloalkyl, S-Ar- C_{0-7} -alkyl, NH- C_{0-7} -alkyl, NH- C_{3-6} -cycloalkyl, NH-Ar- C_{0-7} -alkyl, $N(C_{0-7}\text{-alkyl})_2$, $N(C_{3-6}\text{-cycloalkyl})_2$ or $N(\text{Ar-}C_{0-7}\text{-alkyl})_2$; or, when part of a CHR^{21} or CR^{21} group, R^{21} may be halogen;
- 10

A is chosen from:

- 15 CH_2 , CHR^{21} , O, S, SO_2 , NR^{22} or N-oxide ($\text{N}\rightarrow\text{O}$), where R^{21} is as defined above; and R^{22} is chosen from C_{0-7} -alkyl, C_{3-6} -cycloalkyl and Ar- C_{0-7} -alkyl;

B, D and G are independently chosen from:

-158-

CR^{21} , where R^{21} is as defined above, or N or N-oxide ($N \rightarrow O$);

E is chosen from:

5. CH_2 , CHR^{21} , O, S, SO_2 , NR^{22} or N-oxide ($N \rightarrow O$), where R^{21} and R^{22} are defined as above;

K is chosen from:

CH_2 , CHR^{22} , where R^{22} is defined as above;

10

J, L, M, R, T, T_2 , T_3 and T_4 are independently chosen from:

CR^{21} where R^{21} is as defined above, or N or N-oxide ($N \rightarrow O$);

15

T_5 is chosen from:

CH or N;

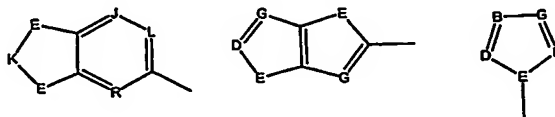
q is a number from one to three, thereby defining a 5-, 6- or 7-membered ring;

20

$R^1 = R^2C(O)$, $R^2OC(O)$, R^2SO_2 , where R^2 is chosen from C_{1-7} -alkyl, C_{3-6} -cycloalkyl or Ar- C_{0-7} -alkyl (when $C = 0$, R^1 is simply an aromatic moiety Ar);

25

provided that when Y is other than $CR^{10}R^{11}-C(O)$ or when U is:



R^1 may also be C_{0-7} -alkyl, C_{3-6} -cycloalkyl or Ar- C_{0-7} -alkyl.

-159-

or a salt, hydrate, solvate, complexe or prodrug thereof.

2. A compound as claimed in claim 1 wherein independently or in combination:

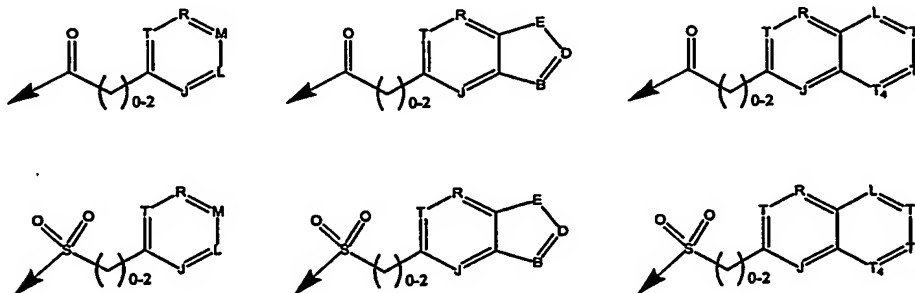
- 5 Z is CH₂;
 P¹ is CH₂;
 P² is CH₂, O or NH;
 R¹ is R²C(O) or R²SO₂.

10 3. A compound as claimed in claim 2, wherein R¹ is R²C(O) or R²SO₂ and R² comprises C₁₋₇-alkyl, C₃₋₆-cycloalkyl or Ar-C₀₋₇-alkyl.

4. A compound as claimed in claim 3 wherein R² comprises Ar-C₀₋₂-alkyl either the carboxamide or sulphonamide.

15

5. A compound as claimed in claim 4, wherein R² is one of:



where J, L, M, R, T, T₂, T₃ and T₄ are independently chosen from CR²¹ where R²¹ is as defined in claim 1, or N or N-oxide (N→O) and B, D and E are as defined in claim 1.

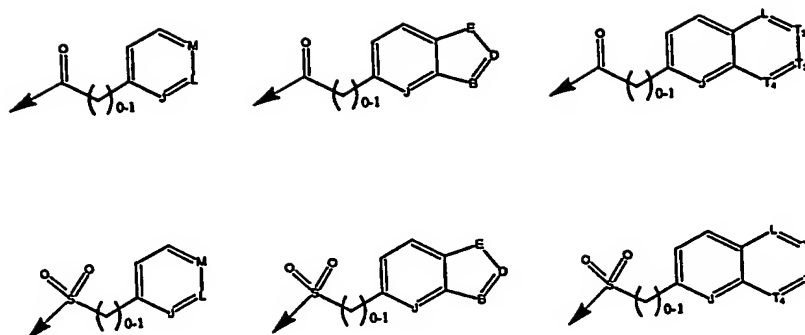
20

6. A compound as claimed in claim 5 wherein R² comprises Ar-C₀₋₁-alkyl either the carboxamide or sulphonamide.

25

7. A compound as claimed in claim 6 wherein R² is:

-160-

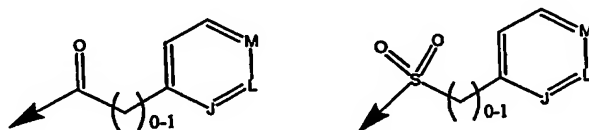


where J, L, M, T₂, T₃ and T₄ are independently chosen from CR²¹ where R²¹ is as defined in claim 1, or N or N-oxide (N→O) and B, D and E are as defined in claim 1.

5

8. A compound as claimed in claim 7 wherein R² comprises a monocyclic Ar-C₀₋₁-alkyl either the carboxamide or sulphonamide.

9. A compound as claimed in claim 8 wherein R² comprises one of:



10

where J, L and M are independently chosen from CR²³ where R²³ is chosen from hydrogen, methyl, methoxy, ethyl, isopropyl, *tert*-butyl, F, Cl, or J, L and M are independently chosen from N or N-oxide (N→O).

15

10. A compound as claimed in claim 1 or claim 2 wherein R¹ comprises:

pyridine-2-sulfonyl;

1-oxy-pyridine-2-sulfonyl;

pyridine-3-sulfonyl;

1-oxy-pyridine-3-sulfonyl;

20

pyridine-2-carbonyl;

1-oxy-pyridine-2-carbonyl;

pyridine-3-carbonyl;

-161-

1-oxy-pyridine-3-carbonyl;

2-pyridine-3-yl-acetyl;

pyridin-2-yl methane sulfonyl;

pyridin-3-yl methane sulfonyl;

5 1-oxy-pyridin-2-yl methane sulfonyl; or

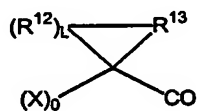
1-oxy-pyridin-3-yl methane sulfonyl.

11. A compound as claimed in any one of claims 1 to 10 wherein Y is CHR^{11}CO ;

10 where R^{11} is selected from C_{0-7} -alkyl or Ar-C_{0-7} -alkyl, (for example hydrogen, a straight or branched alkyl chain, a straight or branched heteroalkyl chain, an optionally substituted arylalkyl chain or an optionally substituted arylheteroalkyl chain); or C_{3-6} -cycloalkyl (for example cyclohexylmethyl or cyclopentylmethyl); or

15

Y is a group:



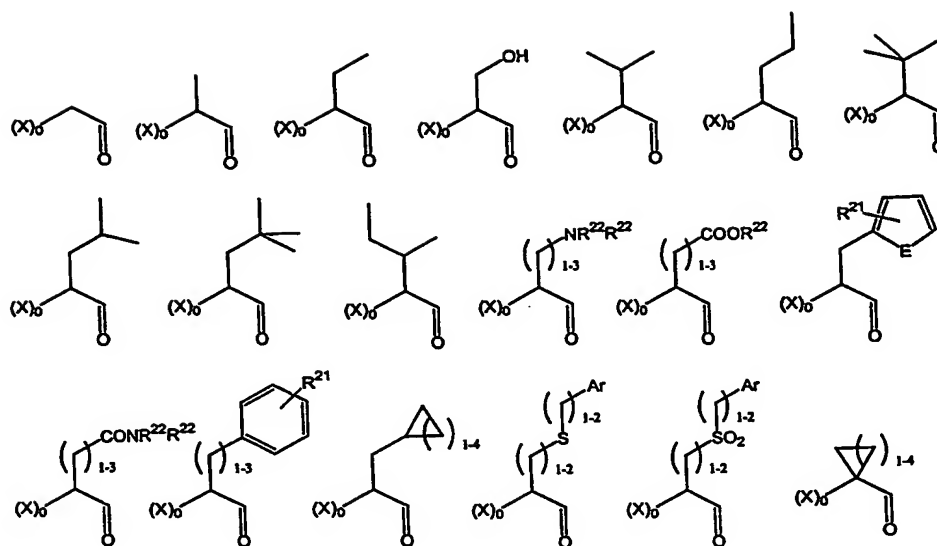
20

where R^{12} and R^{13} are each $\text{CR}^{14}\text{R}^{15}$ and each R^{14} and R^{15} is, independently, selected from C_{0-7} -alkyl or Ar-C_{0-7} -alkyl, (for example hydrogen, a straight or branched alkyl chain, a straight or branched heteroalkyl chain, an optionally substituted arylalkyl chain or an optionally substituted arylheteroalkyl chain) and L is a number from one to four.

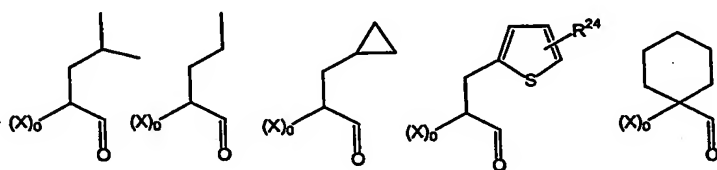
25

12. A compound as claimed in claim 11 where Y is one of the following:

-162-



wherein E, R²¹, R²² and Ar are as defined in claim 1; or



5

wherein R²⁴ is chosen from hydrogen, methyl, methoxy, ethyl, isopropyl, F, Cl.

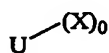
13. A compound as claimed in any one of claims 1 to 12 wherein, in the group (X)₀, each of R¹⁶ and R¹⁷ is selected from C₀₋₇-alkyl or Ar-C₀₋₇-alkyl, for example hydrogen, a straight or branched alkyl chain, a straight or branched heteroalkyl chain, an optionally substituted arylalkyl chain or an optionally substituted arylheteroalkyl chain.

14. A compound as claimed in claim 13, wherein R¹⁶ is hydrogen and R¹⁷ is chosen from hydrogen or C₁₋₄-alkyl, which may be substituted with OH, NR²²R²²,

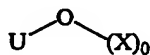
-163-

COOR²², or CONR²²; or Ar-C₁₋₄-alkyl, where the aryl group may be substituted with R²¹, wherein each R²¹ and R²² is independently as defined in claim 1.

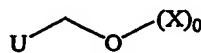
15. A compound as claimed in claim 14 wherein R¹⁶ is hydrogen and R¹⁷ is hydrogen or an unsubstituted C₁₋₄-alkyl group such as methyl, ethyl, propyl, butyl.
16. A compound as claimed in claim 15, wherein R¹⁶ and R¹⁷ are hydrogen and o is zero or one.
17. A compound as claimed in any one of claims 1 to 16 wherein, in the group (W)_n, W is chosen from O, S, SO₂, S(O), C(O) or NR¹⁸, where R¹⁸ is chosen from C₀₋₇-alkyl; and n is 0 or 1.
18. A compound as claimed in claim 17 wherein W is NH where n = 0 or 1.
19. A compound as claimed in any one of claims 1 to 18 wherein, in the group (V)_m, V is chosen from C(O), OC(O), NHC(O), C(O)NH or CHR²⁰, where R²⁰ is C₀₋₄-alkyl and m is 0 or 1.
20. A compound as claimed in any one of claims 1 to 19 wherein the combined V and W substituent is chosen from one of:



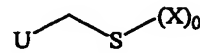
'n' = 0
'm' = 0



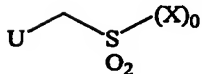
'n' = 1
'W' = O
'm' = 0



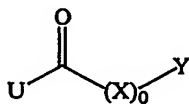
'n' = 1
'W' = O
'V' = CH₂
'm' = 1



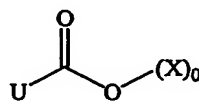
'n' = 1
'W' = S
'V' = CH₂
'm' = 1



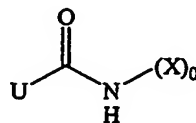
'n' = 1
'W' = SO₂
'V' = CH₂
'm' = 1



'n' = 1
'W' = C(O)
'm' = 0



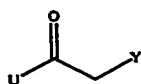
'n' = 1
'W' = O
'V' = C(O)
'm' = 1



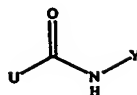
'n' = 1
'W' = NR¹⁸, R¹⁸ = 'H'
'V' = C(O)
'm' = 1

-164-

21. A compound as claimed in claim 20 where the combined V, W and X substituent is chosen from:

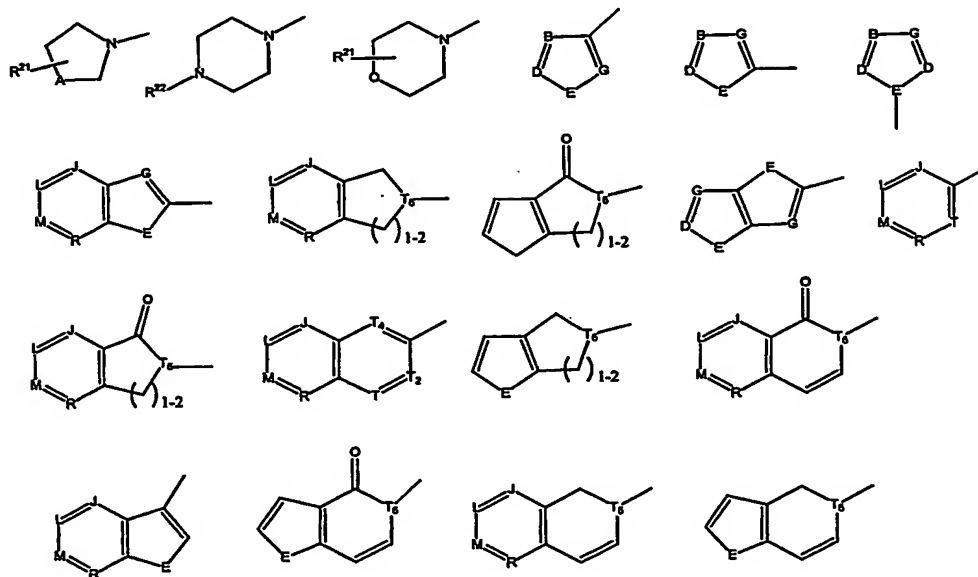


$(X)_0 = \text{'CH}_2\text{'}$
 $\text{'n'} = 1$
 $\text{'W'} = \text{C(O)}$
 $\text{'m'} = 0$



$(X)_0 = \text{'N'}$
 $\text{'n'} = 1$
 $\text{'W'} = \text{NR}^{18}, \text{R}^{18} = \text{'H'}$
 $\text{'V'} = \text{C(O)}$
 $\text{'m'} = 1$

5 22. A compound as claimed in any one of claims 1 to 21 the group U comprises one of the following:



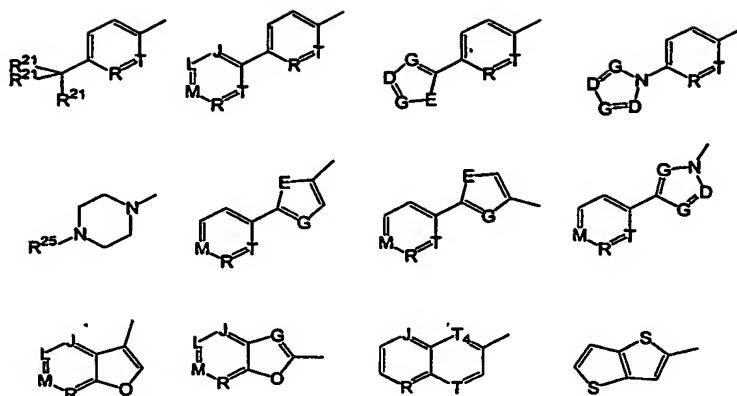
wherein R^{21} , R^{22} , A, B, D, E, G, J, L, M, R, T, T_2 , T_4 and T_5 are as defined in claim 1.

10

23. A compound as claimed in claim 22 wherein U comprises one of the following:

15

-165-



wherein R^{21} , D, E, G, J, L, M, R, T and T_4 are as defined previously.

24. (3a*R*,6a*S*) N-{3-Methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

(3a*R*,6a*S*) N-{3-Methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*c*]pyrazole-1-carbonyl]-butyl}-benzamide;

(3a*S*, 6a*S*) N-{3-Methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-2-oxa-1,4-diaza-pentalene-1-carbonyl]-butyl}-benzamide.

Naphthalene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

Quinoline-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

Benzo[*b*]thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

Benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

Biphenyl-4-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

4-*tert*-Butyl-N-{3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

- 4-Dimethylamino-N-{3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 5 7-Methoxy-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- {3-Methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-carbamic acid benzyl ester;
- 10 5-Methoxy-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thieno[3,2-*b*]thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 3-Methyl-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 20 Quinoxaline-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzo[1,3]dioxole-5-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 25 Quinoline-6-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Furan-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 Thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 35 N-{3-Methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethyl-benzamide;
- Furan-3-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 Thiophene-3-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 N-{3-Methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-phenoxy-benzamide;
- N-{3-Methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-(4-methyl-piperazin-1-yl)-benzamide;

-167-

- 4-Methyl-N-{3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 5 4-Methoxy-N-{3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Isopropyl-N-{3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 10 N-{3-Methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-vinyl-benzamide;
- 15 4-Imidazol-1-yl-N-{3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- N-{3-Methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-thiophen-2-yl-benzamide;
- 20 N-{3-Methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-oxazol-5-yl-benzamide;
- 5-Phenyl-thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 25 N-{3-Methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethoxy-benzamide;
- 5-Pyridin-2-yl-thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 4-Difluoromethoxy-N-{3-methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 35 N-{3-Methyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-morpholin-4-yl-benzamide;
- Naphthalene-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 Quinoline-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzo[*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 Benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

-168-

- Biphenyl-4-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 4-*tert*-Butyl-N-{1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Dimethylamino-N-{1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 10 7-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-carbamic acid benzyl ester;
- 15 5-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 20 Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 3-Methyl-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 25 Quinoxaline-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzo[1,3]dioxole-5-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 Quinoline-6-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 35 Furan-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 N-{1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethyl-benzamide;
- Furan-3-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 Thiophene-3-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

- N-{1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-phenoxy-benzamide;
- 5 N-{1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-(4-methyl-piperazin-1-yl)-benzamide;
- 4-Methyl-N-{1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 10 4-Methoxy-N-{1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Isopropyl-N-{1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 15 N-{1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-vinyl-benzamide;
- 20 4-Imidazol-1-yl-N-{1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- N-{1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-thiophen-2-yl-benzamide;
- 25 N-{1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-oxazol-5-yl-benzamide;
- 5-Phenyl-thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 N-{1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethoxy-benzamide;
- 35 5-Pyridin-2-yl-thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 4-Difluoromethoxy-N-{1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 40 N-{1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-morpholin-4-yl-benzamide;
- Naphthalene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 Quinoline-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

- Benzo[b]thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 Benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Biphenyl-4-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 4-*tert*-Butyl-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Dimethylamino-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 15 7-Methoxy-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 20 {3-Methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-carbamic acid benzyl ester;
- 5-Methoxy-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 25 Thieno[3,2-*b*]thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 3-Methyl-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 Quinoxaline-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 35 Benzo[1,3]dioxole-5-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Quinoline-6-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 Furan-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethyl-benzamide;

-171-

- Furan-3-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 Thiophene-3-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-phenoxy-benzamide;
- 10 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-(4-methyl-piperazin-1-yl)-benzamide;
- 4-Methyl-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 15 4-Methoxy-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Isopropyl-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 20 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-vinyl-benzamide;
- 25 4-Imidazol-1-yl-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-thiophen-2-yl-benzamide;
- 30 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-oxazol-5-yl-benzamide;
- 5-Phenyl-thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 35 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethoxy-benzamide;
- 40 5-Pyridin-2-yl-thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 4-Difluoromethoxy-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 45 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-morpholin-4-yl-benzamide;

-172-

- Naphthalene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 Quinoline-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzo[*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 Benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Biphenyl-4-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 4-*tert*-Butyl-N-{1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Dimethylamino-N-{1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 20 7-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 25 {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-carbamic acid benzyl ester;
- 5-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 3-Methyl-benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 35 Quinoxaline-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 Benzo[1,3]dioxole-5-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Quinoline-6-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 Furan-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

-173-

Thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

5 N-{1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethyl-benzamide;

Furan-3-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

10 Thiophene-3-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

15 N-{1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-phenoxy-benzamide;

N-{1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-(4-methyl-piperazin-1-yl)-benzamide;

20 4-Methyl-N-{1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

4-Methoxy-N-{1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

25 4-Isopropyl-N-{1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

30 N-{1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-vinyl-benzamide;

4-Imidazol-1-yl-N-{1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

35 N-{1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-thiophen-2-yl-benzamide;

N-{1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-oxazol-5-yl-benzamide;

40 5-Phenyl-thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

45 N-{1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethoxy-benzamide;

5-Pyridin-2-yl-thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

- 4-Difluoromethoxy-N-{1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 5 N-{1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-morpholin-4-yl-benzamide;
- Naphthalene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 Quinoline-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzo[*b*]thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 Benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 20 Biphenyl-4-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 4-*tert*-Butyl-N-{3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 25 4-Dimethylamino-N-{3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 7-Methoxy-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 {3-Methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-carbamic acid benzyl ester;
- 35 5-Methoxy-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thieno[3,2-*b*]thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 3-Methyl-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Quinoxaline-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 Benzo[1,3]dioxole-5-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

-175-

- Quinoline-6-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 Furan-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 N-{3-Methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethyl-benzamide;
- Furan-3-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 Thiophene-3-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 20 N-{3-Methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-phenoxy-benzamide;
- N-{3-Methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-(4-methyl-piperazin-1-yl)-benzamide;
- 25 4-Methyl-N-{3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Methoxy-N-{3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 30 4-Isopropyl-N-{3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 35 N-{3-Methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-vinyl-benzamide;
- 4-Imidazol-1-yl-N-{3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 40 N-{3-Methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-thiophen-2-yl-benzamide;
- N-{3-Methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-oxazol-5-yl-benzamide;
- 45 5-Phenyl-thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

-176-

- N-{3-Methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethoxy-benzamide;
- 5 5-Pyridin-2-yl-thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 4-Difluoromethoxy-N-{3-methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 10 N-{3-Methyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-morpholin-4-yl-benzamide;
- Naphthalene-2-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 Quinoline-2-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 20 Benzo[*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 25 Biphenyl-4-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 4-*tert*-Butyl-N-{1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 30 4-Dimethylamino-N-{1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 35 7-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-carbamic acid benzyl ester;
- 40 5-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 3-Methyl-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

-177-

- Quinoxaline-2-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 Benzo[1,3]dioxole-5-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Quinoline-6-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 Furan-2-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 N-{1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethyl-benzamide;
- Furan-3-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 20 Thiophene-3-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- N-{1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-phenoxy-benzamide;
- 25 N-{1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-(4-methyl-piperazin-1-yl)-benzamide;
- 30 4-Methyl-N-{1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Methoxy-N-{1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 35 4-Isopropyl-N-{1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- N-{1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-vinyl-benzamide;
- 40 4-Imidazol-1-yl-N-{1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 45 N-{1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-thiophen-2-yl-benzamide;

-178-

- N-{1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-oxazol-5-yl-benzamide;
- 5 5-Phenyl-thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- N-{1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethoxy-benzamide;
- 10 5-Pyridin-2-yl-thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 4-Difluoromethoxy-N-{1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 15 N-{1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-morpholin-4-yl-benzamide;
- 20 Naphthalene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Quinoline-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 25 Benzo[*b*]thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 Biphenyl-4-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 4-*tert*-Butyl-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 35 4-Dimethylamino-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 40 7-Methoxy-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- {3-Methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-carbamic acid benzyl ester;
- 45 5-Methoxy-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

- Thieno[3,2-*b*]thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 3-Methyl-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Quinoxaline-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 Benzo[1,3]dioxole-5-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Quinoline-6-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 Furan-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 20 Thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethyl-benzamide;
- 25 Furan-3-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thiophene-3-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-phenoxy-benzamide;
- N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-(4-methyl-piperazin-1-yl)-benzamide;
- 35 4-Methyl-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 40 4-Methoxy-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Isopropyl-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 45 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-vinyl-benzamide;

- 4-Imidazol-1-yl-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 5 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-thiophen-2-yl-benzamide;
- N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-oxazol-5-yl-benzamide;
- 10 5-Phenyl-thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethoxy-benzamide;
- 15 5-Pyridin-2-yl-thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 20 4-Difluoromethoxy-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-morpholin-4-yl-benzamide;
- 25 Naphthalene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Quinoline-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 Benzo[*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 35 Benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Biphenyl-4-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 4-*tert*-Butyl-N-{1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Dimethylamino-N-{1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 45 7-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

-181-

- {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-carbamic acid benzyl ester;
- 5 5-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 3-Methyl-benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Quinoxaline-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 Benzo[1,3]dioxole-5-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Quinoline-6-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 20 Furan-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 25 Thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- N-{1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethyl-benzamide;
- 30 Furan-3-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thiophene-3-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 35 N-{1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-phenoxy-benzamide;
- 40 N-{1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-(4-methyl-piperazin-1-yl)-benzamide;
- 4-Methyl-N-{1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 45 4-Methoxy-N-{1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

- 4-Isopropyl-N-{1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 5 N-{1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-vinyl-benzamide;
- 4-Imidazol-1-yl-N-{1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 10 N-{1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-thiophen-2-yl-benzamide;
- N-{1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-oxazol-5-yl-benzamide;
- 15 5-Phenyl-thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 20 N-{1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethoxy-benzamide;
- 5-Pyridin-2-yl-thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 25 4-Difluoromethoxy-N-{1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- N-{1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-morpholin-4-yl-benzamide;
- 30 Naphthalene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 35 Quinoline-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzo[*b*]thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 Benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Biphenyl-4-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 4-*tert*-Butyl-N-{3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

-183-

- 4-Dimethylamino-N-{3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 5 7-Methoxy-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- {3-Methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-carbamic acid benzyl ester;
- 10 5-Methoxy-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 Thieno[3,2-*b*]thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 3-Methyl-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 20 Quinoxaline-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzo[1,3]dioxole-5-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 25 Quinoline-6-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Furan-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 Thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 35 N-{3-Methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethyl-benzamide;
- Furan-3-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 Thiophene-3-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- N-{3-Methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-phenoxy-benzamide;
- 45 N-{3-Methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-(4-methyl-piperazin-1-yl)-benzamide;

- 4-Methyl-N-{3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 5 4-Methoxy-N-{3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Isopropyl-N-{3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 10 N-{3-Methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-vinyl-benzamide;
- 15 4-Imidazol-1-yl-N-{3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- N-{3-Methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-thiophen-2-yl-benzamide;
- 20 N-{3-Methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-oxazol-5-yl-benzamide;
- 5-Phenyl-thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 25 N-{3-Methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethoxy-benzamide;
- 5-Pyridin-2-yl-thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 4-Difluoromethoxy-N-{3-methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 35 N-{3-Methyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-morpholin-4-yl-benzamide;
- Naphthalene-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 Quinoline-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzo[*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 Benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

- Biphenyl-4-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 4-*tert*-Butyl-N-{1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Dimethylamino-N-{1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 10 7-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-carbamic acid benzyl ester;
- 15 5-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 20 Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 3-Methyl-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 25 Quinoxaline-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzo[1,3]dioxole-5-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 Quinoline-6-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 35 Furan-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 N-{1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethyl-benzamide;
- Furan-3-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 Thiophene-3-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

-186-

- N-{1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-phenoxy-benzamide;
- 5 N-{1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-(4-methyl-piperazin-1-yl)-benzamide;
- 4-Methyl-N-{1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 10 4-Methoxy-N-{1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Isopropyl-N-{1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 15 N-{1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-vinyl-benzamide;
- 20 4-Imidazol-1-yl-N-{1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- N-{1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-thiophen-2-yl-benzamide;
- 25 N-{1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-oxazol-5-yl-benzamide;
- 5-Phenyl-thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 N-{1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethoxy-benzamide;
- 35 5-Pyridin-2-yl-thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 4-Difluoromethoxy-N-{1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 40 N-{1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-morpholin-4-yl-benzamide;
- Naphthalene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 Quinoline-2-carboxylic acid {3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

-187-

- Benzo[b]thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 Benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Biphenyl-4-carboxylic acid {3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 4-*tert*-Butyl-N-{3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Dimethylamino-N-{3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 15 7-Methoxy-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 20 {3-Methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-carbamic acid benzyl ester;
- 5-Methoxy-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 25 Thieno[3,2-*b*]thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 3-Methyl-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 Quinoxaline-2-carboxylic acid {3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzo[1,3]dioxole-5-carboxylic acid {3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 35 Quinoline-6-carboxylic acid {3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 Furan-2-carboxylic acid {3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 N-{3-Methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethyl-benzamide;

-188-

- Furan-3-carboxylic acid {3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 Thiophene-3-carboxylic acid {3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- N-{3-Methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-phenoxy-benzamide;
- 10 N-{3-Methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-(4-methyl-piperazin-1-yl)-benzamide;
- 4-Methyl-N-{3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 15 4-Methoxy-N-{3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Isopropyl-N-{3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 20 N-{3-Methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-vinyl-benzamide;
- 25 4-Imidazol-1-yl-N-{3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- N-{3-Methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-thiophen-2-yl-benzamide;
- 30 N-{3-Methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-oxazol-5-yl-benzamide;
- 5-Phenyl-thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 35 N-{3-Methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethoxy-benzamide;
- 40 5-Pyridin-2-yl-thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 4-Difluoromethoxy-N-{3-methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 45 N-{3-Methyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-morpholin-4-yl-benzamide;

-189-

Naphthalene-2-carboxylic acid {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

5 Quinoline-2-carboxylic acid {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

Benzo[*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

10 Benzofuran-2-carboxylic acid {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

15 Biphenyl-4-carboxylic acid {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

4-*tert*-Butyl-N-{1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

20 4-Dimethylamino-N-{1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

7-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

25 {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-carbamic acid benzyl ester;

30 5-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

35 3-Methyl-benzofuran-2-carboxylic acid {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

Quinoxaline-2-carboxylic acid {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

40 Benzo[1,3]dioxole-5-carboxylic acid {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

Quinoline-6-carboxylic acid {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

45 Furan-2-carboxylic acid {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

-190-

- Thiophene-2-carboxylic acid {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 N-{1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethyl-benzamide;
- Furan-3-carboxylic acid {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 Thiophene-3-carboxylic acid {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- N-{1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-phenoxy-benzamide;
- 15 N-{1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-(4-methyl-piperazin-1-yl)-benzamide;
- 4-Methyl-N-{1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 20 4-Methoxy-N-{1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Isopropyl-N-{1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 25 N-{1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-vinyl-benzamide;
- 30 4-Imidazol-1-yl-N-{1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- N-{1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-thiophen-2-yl-benzamide;
- 35 N-{1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-oxazol-5-yl-benzamide;
- 40 5-Phenyl-thiophene-2-carboxylic acid {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- N-{1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethoxy-benzamide;
- 45 5-Pyridin-2-yl-thiophene-2-carboxylic acid {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

-191-

- 4-Difluoromethoxy-N-{1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 5 N-{1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-morpholin-4-yl-benzamide;
- Naphthalene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 Quinoline-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzo[*b*]thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 Benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 20 Biphenyl-4-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 4-*tert*-Butyl-N-{3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 25 4-Dimethylamino-N-{3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 7-Methoxy-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 {3-Methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-carbamic acid benzyl ester;
- 35 5-Methoxy-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thieno[3,2-*b*]thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 3-Methyl-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Quinoxaline-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 Benzo[1,3]dioxole-5-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

-192-

- Quinoline-6-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 Furan-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 N-{3-Methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethyl-benzamide;
- Furan-3-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 Thiophene-3-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 20 N-{3-Methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-phenoxy-benzamide;
- N-{3-Methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-(4-methyl-piperazin-1-yl)-benzamide;
- 25 4-Methyl-N-{3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Methoxy-N-{3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 30 4-Isopropyl-N-{3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 35 N-{3-Methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-vinyl-benzamide;
- 4-Imidazol-1-yl-N-{3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 40 N-{3-Methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-thiophen-2-yl-benzamide;
- N-{3-Methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-oxazol-5-yl-benzamide;
- 45 5-Phenyl-thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

-193-

- N-{3-Methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethoxy-benzamide;
- 5 5-Pyridin-2-yl-thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 4-Difluoromethoxy-N-{3-methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 10 N-{3-Methyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-morpholin-4-yl-benzamide;
- 15 Naphthalene-2-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Quinoline-2-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 20 Benzo[*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 25 Biphenyl-4-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 4-*tert*-Butyl-N-{1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Dimethylamino-N-{1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 35 7-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-carbamic acid benzyl ester;
- 40 5-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 3-Methyl-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

-194-

- Quinoxaline-2-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 Benzo[1,3]dioxole-5-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Quinoline-6-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 Furan-2-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 N-{1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethyl-benzamide;
- 20 Furan-3-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thiophene-3-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 25 N-{1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-phenoxy-benzamide;
- N-{1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-(4-methyl-piperazin-1-yl)-benzamide;
- 30 4-Methyl-N-{1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Methoxy-N-{1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 35 4-Isopropyl-N-{1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 40 N-{1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-vinyl-benzamide;
- 4-Imidazol-1-yl-N-{1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 45 N-{1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-thiophen-2-yl-benzamide;

-195-

- N-{1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-oxazol-5-yl-benzamide;
- 5 5-Phenyl-thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- N-{1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethoxy-benzamide;
- 10 5-Pyridin-2-yl-thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 4-Difluoromethoxy-N-{1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 15 N-{1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-morpholin-4-yl-benzamide;
- 20 Naphthalene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Quinoline-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 25 Benzo[*b*]thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 Biphenyl-4-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 4-*tert*-Butyl-N-{3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 35 4-Dimethylamino-N-{3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 40 7-Methoxy-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- {3-Methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-carbamic acid benzyl ester;
- 45 5-Methoxy-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

- Thieno[3,2-*b*]thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 3-Methyl-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Quinoxaline-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 Benzo[1,3]dioxole-5-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Quinoline-6-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 Furan-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 20 Thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- N-{3-Methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethyl-benzamide;
- 25 Furan-3-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thiophene-3-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 N-{3-Methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-phenoxy-benzamide;
- N-{3-Methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-(4-methyl-piperazin-1-yl)-benzamide;
- 35 4-Methyl-N-{3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 40 4-Methoxy-N-{3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Isopropyl-N-{3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 45 N-{3-Methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-vinyl-benzamide;

-197-

- 4-Imidazol-1-yl-N-{3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 5 N-{3-Methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-thiophen-2-yl-benzamide;
- N-{3-Methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-oxazol-5-yl-benzamide;
- 10 5-Phenyl-thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- N-{3-Methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethoxy-benzamide;
- 15 5-Pyridin-2-yl-thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 4-Difluoromethoxy-N-{3-methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 20 N-{3-Methyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-morpholin-4-yl-benzamide;
- 25 Naphthalene-2-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Quinoline-2-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 Benzo[*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 35 Biphenyl-4-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 4-*tert*-Butyl-N-{1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Dimethylamino-N-{1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 45 7-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

-198-

- {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-carbamic acid benzyl ester;
- 5 5-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 3-Methyl-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Quinoxaline-2-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 Benzo[1,3]dioxole-5-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 20 Quinoline-6-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Furan-2-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 25 Thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- N-{1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethyl-benzamide;
- 30 Furan-3-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 35 Thiophene-3-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- N-{1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-phenoxy-benzamide;
- 40 N-{1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-(4-methyl-piperazin-1-yl)-benzamide;
- 45 4-Methyl-N-{1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Methoxy-N-{1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

-199-

- 4-Isopropyl-N-{1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 5 N-{1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-vinyl-benzamide;
- 4-Imidazol-1-yl-N-{1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 10 N-{1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-thiophen-2-yl-benzamide;
- N-{1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-oxazol-5-yl-benzamide;
- 15 5-Phenyl-thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 20 N-{1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethoxy-benzamide;
- 5-Pyridin-2-yl-thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 25 4-Difluoromethoxy-N-{1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- N-{1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-morpholin-4-yl-benzamide;
- 30 Naphthalene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 35 Quinoline-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzo[*b*]thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 Benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Biphenyl-4-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 4-*tert*-Butyl-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

-200-

- 4-Dimethylamino-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 5 7-Methoxy-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- {3-Methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-carbamic acid benzyl ester;
- 10 5-Methoxy-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 Thieno[3,2-*b*]thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 3-Methyl-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 20 Quinoxaline-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzo[1,3]dioxole-5-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 25 Quinoline-6-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Furan-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 Thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 35 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethyl-benzamide;
- Furan-3-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 Thiophene-3-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-phenoxy-benzamide;
- 45 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-(4-methyl-piperazin-1-yl)-benzamide;

-201-

- 4-Methyl-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 5 4-Methoxy-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Isopropyl-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 10 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-vinyl-benzamide;
- 15 4-Imidazol-1-yl-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-thiophen-2-yl-benzamide;
- 20 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-oxazol-5-yl-benzamide;
- 5-Phenyl-thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 25 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethoxy-benzamide;
- 5-Pyridin-2-yl-thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 4-Difluoromethoxy-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 35 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-morpholin-4-yl-benzamide;
- Naphthalene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 Quinoline-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 Benzo[*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

- Biphenyl-4-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 4-*tert*-Butyl-N-{1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Dimethylamino-N-{1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 10 7-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-carbamic acid benzyl ester;
- 5-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 20 Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 3-Methyl-benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 25 Quinoxaline-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 Benzo[1,3]dioxole-5-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Quinoline-6-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 35 Furan-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 N-{1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethyl-benzamide;
- 45 Furan-3-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thiophene-3-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

-203-

- N-{1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-phenoxy-benzamide;
- 5 N-{1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-(4-methyl-piperazin-1-yl)-benzamide;
- 4-Methyl-N-{1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 10 4-Methoxy-N-{1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 15 4-Isopropyl-N-{1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- N-{1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-vinyl-benzamide;
- 20 4-Imidazol-1-yl-N-{1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- N-{1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-thiophen-2-yl-benzamide;
- 25 N-{1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-oxazol-5-yl-benzamide;
- 30 5-Phenyl-thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- N-{1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethoxy-benzamide;
- 35 5-Pyridin-2-yl-thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 4-Difluoromethoxy-N-{1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 40 N-{1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-morpholin-4-yl-benzamide;
- 45 Naphthalene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Quinoline-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

- Benzo[b]thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 Benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Biphenyl-4-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 4-*tert*-Butyl-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 15 4-Dimethylamino-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 7-Methoxy-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 20 {3-Methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-carbamic acid benzyl ester;
- 5-Methoxy-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 25 Thieno[3,2-*b*]thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 3-Methyl-benzofuran-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 30 Quinoxaline-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 35 Benzo[1,3]dioxole-5-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Quinoline-6-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 Furan-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethyl-benzamide;

- Furan-3-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 Thiophene-3-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-phenoxy-benzamide;
- 15 4-Methyl-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Methoxy-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 20 4-Isopropyl-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 25 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-vinyl-benzamide;
- 4-Imidazol-1-yl-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 30 N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-thiophen-2-yl-benzamide;
- N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-oxazol-5-yl-benzamide;
- 35 5-Phenyl-thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethoxy-benzamide;
- 40 5-Pyridin-2-yl-thiophene-2-carboxylic acid {3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 4-Difluoromethoxy-N-{3-methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;

-206-

- N-{3-Methyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-morpholin-4-yl-benzamide;
- 5 Naphthalene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Quinoline-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 10 Benzo[*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzo[*f*]uran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 Biphenyl-4-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 4-*tert*-Butyl-N-{1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 20 4-Dimethylamino-N-{1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 25 7-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-carbamic acid benzyl ester;
- 30 5-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 35 Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 3-Methyl-benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 40 Quinoxaline-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Benzo[1,3]dioxole-5-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 Quinoline-6-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

-207-

- Furan-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 Thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- N-{1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethyl-benzamide;
- 10 Furan-3-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thiophene-3-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 15 N-{1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-phenoxy-benzamide;
- N-{1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-(4-methyl-piperazin-1-yl)-benzamide;
- 20 4-Methyl-N-{1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 25 4-Methoxy-N-{1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 4-Isopropyl-N-{1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 30 N-{1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-vinyl-benzamide;
- 4-Imidazol-1-yl-N-{1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- 35 N-{1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-thiophen-2-yl-benzamide;
- 40 N-{1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-oxazol-5-yl-benzamide;
- 5-Phenyl-thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 N-{1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-trifluoromethoxy-benzamide;

-208-

- 5-Pyridin-2-yl-thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 4-Difluoromethoxy-N-{1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-benzamide;
- N-{1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-4-morpholin-4-yl-benzamide;
- 10 4-*tert*-Butyl-N-{1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-benzamide;
- 5-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 15 Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 20 3-Methyl-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- N-{1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-4-phenoxy-benzamide;
- 25 N-{1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-4-thiophen-2-yl-benzamide;
- 4-*tert*-Butyl-N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 30 5-Methoxy-benzofuran-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 35 3-Methyl-benzofuran-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 40 N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-4-phenoxy-benzamide;
- N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-4-thiophen-2-yl-benzamide;
- 45 4-*tert*-Butyl-N-{2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-benzamide;

-209-

- 5-Methoxy-benzofuran-2-carboxylic acid {2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 5 Thieno[3,2-*b*]thiophene-2-carboxylic acid {2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 10 3-Methyl-benzofuran-2-carboxylic acid {2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- N-{2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-4-phenoxy-benzamide;
- 15 N-{2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-4-thiophen-2-yl-benzamide;
- 4-*tert*-Butyl-N-{1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-benzamide;
- 20 5-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 25 Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 3-Methyl-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 30 N-{1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-4-phenoxy-benzamide;
- N-{1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-4-thiophen-2-yl-benzamide;
- 35 4-*tert*-Butyl-N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 40 5-Methoxy-benzofuran-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 45 3-Methyl-benzofuran-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;

-210-

- N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-4-phenoxy-benzamide;
- 5 N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-4-thiophen-2-yl-benzamide;
- 4-*tert*-Butyl-N-{2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-benzamide;
- 10 5-Methoxy-benzofuran-2-carboxylic acid {2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 15 Thieno[3,2-*b*]thiophene-2-carboxylic acid {2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 3-Methyl-benzofuran-2-carboxylic acid {2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 20 N-{2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-4-phenoxy-benzamide;
- 25 N-{2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-4-thiophen-2-yl-benzamide;
- 4-*tert*-Butyl-N-{1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-benzamide;
- 30 5-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 35 3-Methyl-benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 40 N-{1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-4-phenoxy-benzamide;
- N-{1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-4-thiophen-2-yl-benzamide;
- 45 4-*tert*-Butyl-N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;

-211-

- 5-Methoxy-benzofuran-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 5 Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 10 3-Methyl-benzofuran-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-4-phenoxy-benzamide;
- 15 N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-4-thiophen-2-yl-benzamide;
- 4-*tert*-Butyl-N-{2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-benzamide;
- 20 5-Methoxy-benzofuran-2-carboxylic acid {2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 25 Thieno[3,2-*b*]thiophene-2-carboxylic acid {2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 30 3-Methyl-benzofuran-2-carboxylic acid {2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- N-{2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-4-phenoxy-benzamide;
- 35 N-{2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-4-thiophen-2-yl-benzamide;
- 40 4-*tert*-Butyl-N-{1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-benzamide;
- 5-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 45 Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;

-212-

- 3-Methyl-benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 5 N-{1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-4-phenoxy-benzamide;
- N-{1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-4-thiophen-2-yl-benzamide;
- 10 4-*tert*-Butyl-N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 15 5-Methoxy-benzofuran-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 20 Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 25 3-Methyl-benzofuran-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-4-phenoxy-benzamide;
- N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-4-thiophen-2-yl-benzamide;
- 30 4-*tert*-Butyl-N-{2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-benzamide;
- 35 5-Methoxy-benzofuran-2-carboxylic acid {2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 40 Thieno[3,2-*b*]thiophene-2-carboxylic acid {2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 3-Methyl-benzofuran-2-carboxylic acid {2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 45 N-{2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-4-phenoxy-benzamide;

-213-

- N-{2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-4-thiophen-2-yl-benzamide;
- 5 4-*tert*-Butyl-N-{1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-benzamide;
- 5-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 10 Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 3-Methyl-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 15 N-{1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-4-phenoxy-benzamide;
- 20 N-{1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-4-thiophen-2-yl-benzamide;
- 4-*tert*-Butyl-N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 25 5-Methoxy-benzofuran-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 30 3-Methyl-benzofuran-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 35 N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-4-phenoxy-benzamide;
- N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-4-thiophen-2-yl-benzamide;
- 40 4-*tert*-Butyl-N-{2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-benzamide;
- 45 5-Methoxy-benzofuran-2-carboxylic acid {2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;

-214-

- Thieno[3,2-*b*]thiophene-2-carboxylic acid {2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 5 3-Methyl-benzofuran-2-carboxylic acid {2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- N-{2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-4-phenoxy-benzamide;
- 10 N-{2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-4-thiophen-2-yl-benzamide;
- 4-*tert*-Butyl-N-{1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-benzamide;
- 15 5-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 20 Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 3-Methyl-benzofuran-2-carboxylic acid {1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 25 N-{1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-4-phenoxy-benzamide;
- N-{1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-4-thiophen-2-yl-benzamide;
- 30 4-*tert*-Butyl-N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 35 5-Methoxy-benzofuran-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 40 3-Methyl-benzofuran-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-4-phenoxy-benzamide;
- 45 N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-4-thiophen-2-yl-benzamide;

- 4-*tert*-Butyl-N-{2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-benzamide;
- 5 5-Methoxy-benzofuran-2-carboxylic acid {2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 10 Thieno[3,2-*b*]thiophene-2-carboxylic acid {2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 15 3-Methyl-benzofuran-2-carboxylic acid {2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 20 N-{2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-4-phenoxy-benzamide;
- 25 4-*tert*-Butyl-N-{1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-benzamide;
- 30 5-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 35 Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 40 3-Methyl-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 45 N-{1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-4-phenoxy-benzamide;
- N-{1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-4-thiophen-2-yl-benzamide;
- 4-*tert*-Butyl-N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;

-216-

- 5-Methoxy-benzofuran-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 5 Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 10 3-Methyl-benzofuran-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 15 N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-4-phenoxy-benzamide;
- 20 4-*tert*-Butyl-N-{2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-benzamide;
- 25 5-Methoxy-benzofuran-2-carboxylic acid {2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 30 Thieno[3,2-*b*]thiophene-2-carboxylic acid {2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 35 3-Methyl-benzofuran-2-carboxylic acid {2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- N-{2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-4-phenoxy-benzamide;
- 40 N-{2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-4-thiophen-2-yl-benzamide;
- 45 4-*tert*-Butyl-N-{1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-benzamide;
- 5-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;

-217-

- Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 5 3-Methyl-benzofuran-2-carboxylic acid {1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 10 N-{1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-4-phenoxy-benzamide;
- N-{1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-4-thiophen-2-yl-benzamide;
- 15 4-*tert*-Butyl-N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 5-Methoxy-benzofuran-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 20 Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 25 3-Methyl-benzofuran-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 30 N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-4-phenoxy-benzamide;
- N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-4-thiophen-2-yl-benzamide;
- 35 4-*tert*-Butyl-N-{2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-benzamide;
- 5-Methoxy-benzofuran-2-carboxylic acid {2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 40 Thieno[3,2-*b*]thiophene-2-carboxylic acid {2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 45

-218-

- 3-Methyl-benzofuran-2-carboxylic acid {2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 5 N-{2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-4-phenoxy-benzamide;
- N-{2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-4-thiophen-2-yl-benzamide;
- 10 4-*tert*-Butyl-N-{1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-benzamide;
- 15 5-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 20 Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- 25 3-Methyl-benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;
- N-{1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-4-phenoxy-benzamide;
- 30 N-{1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-4-thiophen-2-yl-benzamide;
- 4-*tert*-Butyl-N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 35 5-Methoxy-benzofuran-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 40 Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 45 3-Methyl-benzofuran-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-4-phenoxy-benzamide;

N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-4-thiophen-2-yl-benzamide;

- 5 4-*tert*-Butyl-N-{2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-benzamide;

- 10 5-Methoxy-benzofuran-2-carboxylic acid {2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;

- 15 Thieno[3,2-*b*]thiophene-2-carboxylic acid {2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;

- 3-Methyl-benzofuran-2-carboxylic acid {2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;

- 20 N-{2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-4-phenoxy-benzamide;

- 25 N-{2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-4-thiophen-2-yl-benzamide;

4-*tert*-Butyl-N-{1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-benzamide;

- 30 5-Methoxy-benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;

- 35 Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;

- 40 3-Methyl-benzofuran-2-carboxylic acid {1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-amide;

N-{1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-4-phenoxy-benzamide;

- 45 N-{1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-cyclohexyl}-4-thiophen-2-yl-benzamide;

-220-

- 4-*tert*-Butyl-N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 5 5-Methoxy-benzofuran-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 10 Thieno[3,2-*b*]thiophene-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 15 3-Methyl-benzofuran-2-carboxylic acid {1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 20 N-{1-cyclopropylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-4-phenoxy-benzamide;
- 25 4-*tert*-Butyl-N-{2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-benzamide;
- 30 5-Methoxy-benzofuran-2-carboxylic acid {2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 35 Thieno[3,2-*b*]thiophene-2-carboxylic acid {2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 40 3-Methyl-benzofuran-2-carboxylic acid {2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-amide;
- 45 N-{2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-4-phenoxy-benzamide;
- 40 N-{2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-1-thiophen-2-ylmethyl-ethyl}-4-thiophen-2-yl-benzamide;
- 45 2-Isobutyl-4-morpholin-4-yl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 2-Isobutyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-piperazin-1-yl-butane-1,4-dione;

-221-

- 2-Isobutyl-4-(4-methyl-piperazin-1-yl)-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 5 2-Isobutyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(4-phenyl-piperazin-1-yl)-butane-1,4-dione;
- 2-Isobutyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(3,4,4a,8a-tetrahydro-1H-isoquinolin-2-yl)-butane-1,4-dione;
- 10 2-Isobutyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(1,3,3a,7a-tetrahydro-isoindol-2-yl)-butane-1,4-dione;
- 15 4-(4-Benzyl-piperazin-1-yl)-2-isobutyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 2-Isobutyl-4-morpholin-4-yl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 20 2-Isobutyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-piperazin-1-yl-butane-1,4-dione;
- 2-Isobutyl-4-(4-methyl-piperazin-1-yl)-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 25 2-Isobutyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(4-phenyl-piperazin-1-yl)-butane-1,4-dione;
- 30 2-Isobutyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(3,4,4a,8a-tetrahydro-1H-isoquinolin-2-yl)-butane-1,4-dione;
- 2-Isobutyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(1,3,3a,7a-tetrahydro-isoindol-2-yl)-butane-1,4-dione;
- 35 4-(4-Benzyl-piperazin-1-yl)-2-isobutyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 2-Isobutyl-4-morpholin-4-yl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 40 2-Isobutyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-piperazin-1-yl-butane-1,4-dione;
- 2-Isobutyl-4-(4-methyl-piperazin-1-yl)-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 45 2-Isobutyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(4-phenyl-piperazin-1-yl)-butane-1,4-dione;

-222-

- 2-Isobutyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(3,4,4a,8a-tetrahydro-1H-isoquinolin-2-yl)-butane-1,4-dione;
- 5 2-Isobutyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(1,3,3a,7a-tetrahydro-isoindol-2-yl)-butane-1,4-dione;
- 4-(4-Benzyl-piperazin-1-yl)-2-isobutyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 10 2-Isobutyl-4-morpholin-4-yl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 15 2-Isobutyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-piperazin-1-yl-butane-1,4-dione;
- 2-Isobutyl-4-(4-methyl-piperazin-1-yl)-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 20 2-Isobutyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(4-phenyl-piperazin-1-yl)-butane-1,4-dione;
- 2-Isobutyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(3,4,4a,8a-tetrahydro-1H-isoquinolin-2-yl)-butane-1,4-dione;
- 25 2-Isobutyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(1,3,3a,7a-tetrahydro-isoindol-2-yl)-butane-1,4-dione;
- 4-(4-Benzyl-piperazin-1-yl)-2-isobutyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 30 2-Isobutyl-4-morpholin-4-yl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 35 2-Isobutyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-piperazin-1-yl-butane-1,4-dione;
- 2-Isobutyl-4-(4-methyl-piperazin-1-yl)-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 40 2-Isobutyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(4-phenyl-piperazin-1-yl)-butane-1,4-dione;
- 2-Isobutyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(3,4,4a,8a-tetrahydro-1H-isoquinolin-2-yl)-butane-1,4-dione;
- 45 2-Isobutyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(1,3,3a,7a-tetrahydro-isoindol-2-yl)-butane-1,4-dione;

-223-

- 4-(4-Benzyl-piperazin-1-yl)-2-isobutyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 5 2-Isobutyl-4-morpholin-4-yl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 2-Isobutyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-piperazin-1-yl-butane-1,4-dione;
- 10 2-Isobutyl-4-(4-methyl-piperazin-1-yl)-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 15 2-Isobutyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(4-phenyl-piperazin-1-yl)-butane-1,4-dione;
- 2-Isobutyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(3,4,4a,8a-tetrahydro-1H-isoquinolin-2-yl)-butane-1,4-dione;
- 20 2-Isobutyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(1,3,3a,7a-tetrahydro-isoindol-2-yl)-butane-1,4-dione;
- 4-(4-Benzyl-piperazin-1-yl)-2-isobutyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 25 2-Isobutyl-4-morpholin-4-yl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 2-Isobutyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-piperazin-1-yl-butane-1,4-dione;
- 30 2-Isobutyl-4-(4-methyl-piperazin-1-yl)-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 35 2-Isobutyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(4-phenyl-piperazin-1-yl)-butane-1,4-dione;
- 2-Isobutyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(3,4,4a,8a-tetrahydro-1H-isoquinolin-2-yl)-butane-1,4-dione;
- 40 2-Isobutyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(1,3,3a,7a-tetrahydro-isoindol-2-yl)-butane-1,4-dione;
- 45 4-(4-Benzyl-piperazin-1-yl)-2-isobutyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 2-Isobutyl-4-morpholin-4-yl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;

-224-

- 2-Isobutyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-piperazin-1-yl-butane-1,4-dione;
- 5 2-Isobutyl-4-(4-methyl-piperazin-1-yl)-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 2-Isobutyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(4-phenyl-piperazin-1-yl)-butane-1,4-dione;
- 10 2-Isobutyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(3,4,4a,8a-tetrahydro-1H-isoquinolin-2-yl)-butane-1,4-dione;
- 15 2-Isobutyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(1,3,3a,7a-tetrahydro-isoindol-2-yl)-butane-1,4-dione;
- 4-(4-Benzyl-piperazin-1-yl)-2-isobutyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 20 2-Isobutyl-4-morpholin-4-yl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 2-Isobutyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-piperazin-1-yl-butane-1,4-dione;
- 25 2-Isobutyl-4-(4-methyl-piperazin-1-yl)-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 30 2-Isobutyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(4-phenyl-piperazin-1-yl)-butane-1,4-dione;
- 2-Isobutyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(3,4,4a,8a-tetrahydro-1H-isoquinolin-2-yl)-butane-1,4-dione;
- 35 2-Isobutyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(1,3,3a,7a-tetrahydro-isoindol-2-yl)-butane-1,4-dione;
- 40 4-(4-Benzyl-piperazin-1-yl)-2-isobutyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 2-Isobutyl-4-morpholin-4-yl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 45 2-Isobutyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-piperazin-1-yl-butane-1,4-dione;

-225-

- 2-Isobutyl-4-(4-methyl-piperazin-1-yl)-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 5 2-Isobutyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(4-phenyl-piperazin-1-yl)-butane-1,4-dione;
- 10 2-Isobutyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(3,4,4a,8a-tetrahydro-1H-isoquinolin-2-yl)-butane-1,4-dione;
- 2-Isobutyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-4-(1,3,3a,7a-tetrahydro-isoindol-2-yl)-butane-1,4-dione;
- 15 4-(4-Benzyl-piperazin-1-yl)-2-isobutyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 4-(2-Biphenyl-3-yl-4-methyl-pentanoyl)-1-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 20 4-(2-Biphenyl-3-yl-4-methyl-pentanoyl)-1-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 25 4-(2-Biphenyl-3-yl-4-methyl-pentanoyl)-1-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 4-(2-Biphenyl-3-yl-4-methyl-pentanoyl)-1-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 30 4-(2-Biphenyl-3-yl-4-methyl-pentanoyl)-1-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 4-(2-Biphenyl-3-yl-4-methyl-pentanoyl)-1-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 35 4-(2-Biphenyl-3-yl-4-methyl-pentanoyl)-1-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 40 4-(2-Biphenyl-3-yl-4-methyl-pentanoyl)-1-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 45 4-(2-Biphenyl-3-yl-4-methyl-pentanoyl)-1-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 4-(2-Biphenyl-3-yl-4-methyl-pentanoyl)-1-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;

-226-

- 4-[4-Methyl-2-(3-pyridin-2-yl-phenyl)-pentanoyl]-1-(pyridine-2-sulfonyl)-
hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 5 4-[4-Methyl-2-(3-pyridin-2-yl-phenyl)-pentanoyl]-1-(pyridine-3-sulfonyl)-
hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 10 4-[4-Methyl-2-(3-pyridin-2-yl-phenyl)-pentanoyl]-1-(1-oxy-pyridine-2-sulfonyl)-
hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 15 4-[4-Methyl-2-(3-pyridin-2-yl-phenyl)-pentanoyl]-1-(pyridine-2-carbonyl)-
hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 20 4-[4-Methyl-2-(3-pyridin-2-yl-phenyl)-pentanoyl]-1-(2-pyridin-3-yl-acetyl)-
hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 25 4-[4-Methyl-2-(3-pyridin-2-yl-phenyl)-pentanoyl]-1-(pyridin-2-
ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 30 4-[4-Methyl-2-(3-pyridin-2-yl-phenyl)-pentanoyl]-1-(pyridin-3-
ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 35 4-[4-Methyl-2-(3-pyridin-2-yl-phenyl)-pentanoyl]-1-(1-oxy-pyridin-2-
ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 40 4-[4-Methyl-2-(3-pyridin-2-yl-phenyl)-pentanoyl]-1-(1-oxy-pyridin-3-
ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 45 4-[4-Methyl-2-(3-pyridin-3-yl-phenyl)-pentanoyl]-1-(pyridine-2-sulfonyl)-
hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 4-[4-Methyl-2-(3-pyridin-3-yl-phenyl)-pentanoyl]-1-(pyridine-3-sulfonyl)-
hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 4-[4-Methyl-2-(3-pyridin-3-yl-phenyl)-pentanoyl]-1-(1-oxy-pyridine-2-sulfonyl)-
hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 4-[4-Methyl-2-(3-pyridin-3-yl-phenyl)-pentanoyl]-1-(1-oxy-pyridine-3-sulfonyl)-
hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 4-[4-Methyl-2-(3-pyridin-3-yl-phenyl)-pentanoyl]-1-(pyridine-2-carbonyl)-
hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 4-[4-Methyl-2-(3-pyridin-3-yl-phenyl)-pentanoyl]-1-(2-pyridin-3-yl-acetyl)-
hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;

-227-

- 4-[4-Methyl-2-(3-pyridin-3-yl-phenyl)-pentanoyl]-1-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 5 4-[4-Methyl-2-(3-pyridin-3-yl-phenyl)-pentanoyl]-1-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 4-[4-Methyl-2-(3-pyridin-3-yl-phenyl)-pentanoyl]-1-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 10 4-[4-Methyl-2-(3-pyridin-3-yl-phenyl)-pentanoyl]-1-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 4-[4-Methyl-2-(3-pyridin-4-yl-phenyl)-pentanoyl]-1-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 15 4-[4-Methyl-2-(3-pyridin-4-yl-phenyl)-pentanoyl]-1-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 4-[4-Methyl-2-(3-pyridin-4-yl-phenyl)-pentanoyl]-1-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 20 4-[4-Methyl-2-(3-pyridin-4-yl-phenyl)-pentanoyl]-1-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 25 4-[4-Methyl-2-(3-pyridin-4-yl-phenyl)-pentanoyl]-1-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 4-[4-Methyl-2-(3-pyridin-4-yl-phenyl)-pentanoyl]-1-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 30 4-[4-Methyl-2-(3-pyridin-4-yl-phenyl)-pentanoyl]-1-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 35 4-[4-Methyl-2-(3-pyridin-4-yl-phenyl)-pentanoyl]-1-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 4-[4-Methyl-2-(3-pyridin-4-yl-phenyl)-pentanoyl]-1-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 40 4-[4-Methyl-2-(3-pyridin-4-yl-phenyl)-pentanoyl]-1-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-3-one;
- 45 Furan-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thiophene-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

-228-

- Benzo[b]thiophene-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 Furan-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Thiophene-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 10 Benzo[b]thiophene-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Naphthalene-1-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 15 Quinoline-8-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 20 4-*tert*-Butyl-N-{1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 4-*tert*-Butyl-N-{1-(4-fluoro-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 25 4-*tert*-Butyl-N-{1-(4-methoxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 30 4-*tert*-Butyl-N-{1-(3-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- Biphenyl-4-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 35 Biphenyl-4-carboxylic acid {1-(4-fluoro-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Biphenyl-4-carboxylic acid {1-(4-methoxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 40 Biphenyl-4-carboxylic acid {1-(3-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 45 Furan-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thiophene-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

- Benzo[b]thiophene-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 Furan-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Thiophene-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 10 Benzo[b]thiophene-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Naphthalene-1-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 15 Quinoline-8-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 20 4-*tert*-Butyl-N- {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 4-*tert*-Butyl-N- {1-(4-fluoro-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 25 4-*tert*-Butyl-N- {1-(4-methoxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 4-*tert*-Butyl-N- {1-(3-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 30 Biphenyl-4-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 35 Biphenyl-4-carboxylic acid {1-(4-fluoro-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Biphenyl-4-carboxylic acid {1-(4-methoxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 40 Biphenyl-4-carboxylic acid {1-(3-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Furan-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 Thiophene-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

-230-

- Benzo[b]thiophene-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 Furan-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Thiophene-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 10 Benzo[b]thiophene-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Naphthalene-1-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 15 Quinoline-8-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 20 4-*tert*-Butyl-N-{1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 4-*tert*-Butyl-N-{1-(4-fluoro-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 25 4-*tert*-Butyl-N-{1-(4-methoxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 4-*tert*-Butyl-N-{1-(3-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 30 Biphenyl-4-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 35 Biphenyl-4-carboxylic acid {1-(4-fluoro-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Biphenyl-4-carboxylic acid {1-(4-methoxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 40 Biphenyl-4-carboxylic acid {1-(3-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Furan-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 Thiophene-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

-231-

- Benzo[b]thiophene-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 Furan-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Thiophene-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 10 Benzo[b]thiophene-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Naphthalene-1-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 15 Quinoline-8-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 20 4-*tert*-Butyl-N-{1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 4-*tert*-Butyl-N-{1-(4-fluoro-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 25 4-*tert*-Butyl-N-{1-(4-methoxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 4-*tert*-Butyl-N-{1-(3-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 30 Biphenyl-4-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 35 Biphenyl-4-carboxylic acid {1-(4-fluoro-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Biphenyl-4-carboxylic acid {1-(4-methoxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 40 Biphenyl-4-carboxylic acid {1-(3-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 45 Furan-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thiophene-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

-232-

- Benzo[b]thiophene-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 Furan-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Thiophene-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 10 Benzo[b]thiophene-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Naphthalene-1-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 15 Quinoline-8-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 20 4-*tert*-Butyl-N- {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 4-*tert*-Butyl-N- {1-(4-fluoro-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 25 4-*tert*-Butyl-N- {1-(4-methoxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 4-*tert*-Butyl-N- {1-(3-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 30 Biphenyl-4-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 35 Biphenyl-4-carboxylic acid {1-(4-fluoro-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Biphenyl-4-carboxylic acid {1-(4-methoxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 40 Biphenyl-4-carboxylic acid {1-(3-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 45 Furan-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thiophene-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

-233-

- Benzo[b]thiophene-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 Furan-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Thiophene-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 10 Benzo[b]thiophene-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Naphthalene-1-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 15 Quinoline-8-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 20 4-*tert*-Butyl-N-{1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 4-*tert*-Butyl-N-{1-(4-fluoro-benzyl)-2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 25 4-*tert*-Butyl-N-{1-(4-methoxy-benzyl)-2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 4-*tert*-Butyl-N-{1-(3-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 30 Biphenyl-4-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Biphenyl-4-carboxylic acid {1-(4-fluoro-benzyl)-2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 35 Biphenyl-4-carboxylic acid {1-(4-methoxy-benzyl)-2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Biphenyl-4-carboxylic acid {1-(3-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 40 Furan-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 45 Thiophene-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

-234-

- Benzo[b]thiophene-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 Furan-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Thiophene-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 10 Benzo[b]thiophene-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 15 Naphthalene-1-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Quinoline-8-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 20 4-*tert*-Butyl-N-{1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 4-*tert*-Butyl-N-{1-(4-fluoro-benzyl)-2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 25 4-*tert*-Butyl-N-{1-(4-methoxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 30 4-*tert*-Butyl-N-{1-(3-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- Biphenyl-4-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 35 Biphenyl-4-carboxylic acid {1-(4-fluoro-benzyl)-2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Biphenyl-4-carboxylic acid {1-(4-methoxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 40 Biphenyl-4-carboxylic acid {1-(3-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 45 Furan-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Thiophene-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

-235-

- Benzo[b]thiophene-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 Furan-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Thiophene-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 10 Benzo[b]thiophene-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 15 Naphthalene-1-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Quinoline-8-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 20 4-*tert*-Butyl-N-{1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 25 4-*tert*-Butyl-N-{1-(4-fluoro-benzyl)-2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 4-*tert*-Butyl-N-{1-(4-methoxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 30 4-*tert*-Butyl-N-{1-(3-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- Biphenyl-4-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 35 Biphenyl-4-carboxylic acid {1-(4-fluoro-benzyl)-2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Biphenyl-4-carboxylic acid {1-(4-methoxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 40 Biphenyl-4-carboxylic acid {1-(3-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 45 Furan-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

- Thiophene-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 Benzo[*b*]thiophene-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Furan-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 10 Thiophene-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 15 Benzo[*b*]thiophene-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Naphthalene-1-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 20 Quinoline-8-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 4-*tert*-Butyl-N-{1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 25 4-*tert*-Butyl-N-{1-(4-fluoro-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 30 4-*tert*-Butyl-N-{1-(4-methoxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 4-*tert*-Butyl-N-{1-(3-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 35 Biphenyl-4-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Biphenyl-4-carboxylic acid {1-(4-fluoro-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 40 Biphenyl-4-carboxylic acid {1-(4-methoxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 45 Biphenyl-4-carboxylic acid {1-(3-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Furan-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;

- Thiophene-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- 5 Benzo[*b*]thiophene-3-carboxylic acid {3,3-dimethyl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrole-1-carbonyl]-butyl}-amide;
- Furan-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 10 Thiophene-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 15 Benzo[*b*]thiophene-3-carboxylic acid {1-cyclohexylmethyl-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Naphthalene-1-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 20 Quinoline-8-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 25 4-*tert*-Butyl-N-{1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 4-*tert*-Butyl-N-{1-(4-fluoro-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 30 4-*tert*-Butyl-N-{1-(4-methoxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- 35 4-*tert*-Butyl-N-{1-(3-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-benzamide;
- Biphenyl-4-carboxylic acid {1-(4-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 40 Biphenyl-4-carboxylic acid {1-(4-fluoro-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- Biphenyl-4-carboxylic acid {1-(4-methoxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;
- 45 Biphenyl-4-carboxylic acid {1-(3-hydroxy-benzyl)-2-oxo-2-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-ethyl}-amide;

-238-

- 2-Cyclohexylmethyl-4-morpholin-4-yl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 5 2-Cyclohexylmethyl-4-morpholin-4-yl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 2-Cyclohexylmethyl-4-morpholin-4-yl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 10 2-Cyclohexylmethyl-4-morpholin-4-yl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 2-Cyclohexylmethyl-4-morpholin-4-yl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 15 2-Cyclohexylmethyl-4-morpholin-4-yl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 2-Cyclohexylmethyl-4-morpholin-4-yl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 20 2-Cyclohexylmethyl-4-morpholin-4-yl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 25 2-Cyclohexylmethyl-4-morpholin-4-yl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 2-Cyclohexylmethyl-4-morpholin-4-yl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 30 2-(2,2-Dimethyl-propyl)-4-morpholin-4-yl-1-[6-oxo-4-(pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 2-(2,2-Dimethyl-propyl)-4-morpholin-4-yl-1-[6-oxo-4-(pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 35 2-(2,2-Dimethyl-propyl)-4-morpholin-4-yl-1-[6-oxo-4-(1-oxy-pyridine-2-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 2-(2,2-Dimethyl-propyl)-4-morpholin-4-yl-1-[6-oxo-4-(1-oxy-pyridine-3-sulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 40 2-(2,2-Dimethyl-propyl)-4-morpholin-4-yl-1-[6-oxo-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;
- 45 2-(2,2-Dimethyl-propyl)-4-morpholin-4-yl-1-[6-oxo-4-(2-pyridin-3-yl-acetyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;

-239-

2-(2,2-Dimethyl-propyl)-4-morpholin-4-yl-1-[6-oxo-4-(pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;

5 2-(2,2-Dimethyl-propyl)-4-morpholin-4-yl-1-[6-oxo-4-(pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione;

2-(2,2-Dimethyl-propyl)-4-morpholin-4-yl-1-[6-oxo-4-(1-oxy-pyridin-2-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione; or

10 2-(2,2-Dimethyl-propyl)-4-morpholin-4-yl-1-[6-oxo-4-(1-oxy-pyridin-3-ylmethanesulfonyl)-hexahydro-pyrrolo[3,2-*b*]pyrrol-1-yl]-butane-1,4-dione.

25. A method of validating a known or putative cysteine protease inhibitor as a therapeutic target, the method comprising:

15

(a) assessing the *in vitro* binding of a compound as claimed in any one of claims 1 to 24 to an isolated known or putative cysteine protease, providing a measure of potency; and optionally, one or more of the steps of:

20

(b) assessing the binding of a compound as claimed in any one of claims 1 to 24 to closely related homologous proteases of the target and general house-keeping proteases (e.g. trypsin) to provides a measure of selectivity;

25

(c) monitoring a cell-based functional marker of a particular cysteine protease activity, in the presence of a compound as claimed in any one of claims 1 to 24; and

30

(d) monitoring an animal model-based functional marker of a particular cysteine protease activity in the presence of a compound as claimed in any one of claims 1 to 24.

26. The use of a compound as claimed in any one of claims 1 to 24 in the validation of a known or putative cysteine protease inhibitor as a therapeutic target.

35

-240-

27. A compound as claimed in any one of claims 1 to 24 for use in medicine, especially for preventing or treating diseases in which the disease pathology may be modified by inhibiting a cysteine protease.

5 28. The use of a compound as claimed in any one of claims 1 to 24 in the preparation of a medicament for preventing or treating diseases in which the disease pathology may be modified by inhibiting a cysteine protease.

10 29. A compound as claimed in any one of claims 1 to 24 for use in the treatment of osteoporosis, Paget's disease, gingival diseases such as gingivitis and periodontitis, hypercalcaemia of malignancy, metabolic bone disease, diseases involving matrix or cartilage degradation, in particular osteoarthritis or rheumatoid arthritis and neoplastic diseases.

15 30. The use of a compound as claimed in any one of claims 1 to 24 in the preparation of a medicament for the treatment of osteoporosis, Paget's disease, gingival diseases such as gingivitis and periodontitis, hypercalcaemia of malignancy, metabolic bone disease, diseases involving matrix or cartilage degradation, in particular osteoarthritis or rheumatoid arthritis and neoplastic
20 diseases.

31. A pharmaceutical or veterinary composition comprising one or more compounds as claimed in any one of claims 1 to 24 and a pharmaceutically or veterinarily acceptable carrier.

25 32. A process for the preparation of a pharmaceutical or veterinary composition as claimed in claim 31, the process comprising bringing the active compound(s) into association with the carrier, for example by admixture.

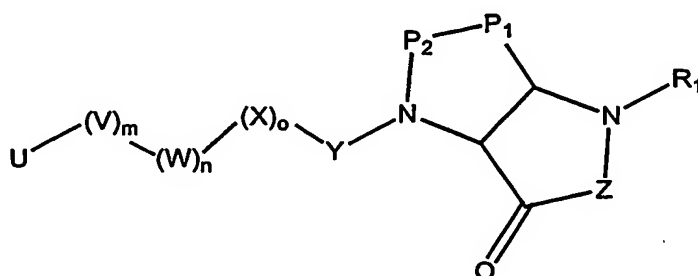
-241-

ABSTRACT

BIOLOGICALLY ACTIVE COMPOUNDS

Compounds of general formula (I)

5



(I)

wherein:

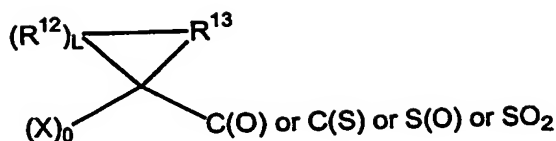
10 $Z = CR^3R^4$, where R^3 and R^4 are independently chosen from C_{0-7} -alkyl (when $C = 0$, R^3 or R^4 is simply a hydrogen atom), C_{3-6} -cycloalkyl, Ar- C_{0-7} -alkyl (when $C = 0$, R^3 or R^4 is simply an aromatic moiety Ar),

15 $P_1 = CR^5R^6$, where R^5 and R^6 are independently chosen from C_{0-7} -alkyl, C_{3-6} -cycloalkyl, Ar- C_{0-7} -alkyl, O- C_{0-7} -alkyl, O- C_{3-6} -cycloalkyl, O-Ar- C_{0-7} -alkyl, S- C_{0-7} -alkyl, S- C_{3-6} -cycloalkyl, S-Ar- C_{0-7} -alkyl, NH- C_{0-7} -alkyl, NH- C_{3-6} -cycloalkyl, NH-Ar- C_{0-7} -alkyl, N(C_{0-7} -alkyl)₂, N(C_{3-6} -cycloalkyl)₂ or N(Ar- C_{0-7} -alkyl)₂;

20 $P_2 = O$, CR^7R^8 or NR^9 , where R^7 and R^8 are independently chosen from C_{0-7} -alkyl, C_{3-6} -cycloalkyl, Ar- C_{0-7} -alkyl and R^9 is chosen from C_{0-7} -alkyl, C_{3-6} -cycloalkyl or Ar- C_{0-7} -alkyl;

25 $Y = CR^{10}R^{11}-C(O)$ or $CR^{10}R^{11}-C(S)$ or $CR^{10}R^{11}-S(O)$ or $CR^{10}R^{11}-SO_2$ where R^{10} and R^{11} are independently chosen from C_{0-7} -alkyl, C_{3-6} -cycloalkyl and Ar- C_{0-7} -alkyl, or Y represents

-242-



5 where L is a number from one to four and R^{12} and R^{13} are independently chosen from $CR^{14}R^{15}$ where R^{14} and R^{15} are independently chosen from C_{0-7} -alkyl, C_{3-6} -cycloalkyl, Ar- C_{0-7} -alkyl or halogen; and for each R^{12} and R^{13} either R^{14} or R^{15} (but not both R^{14} and R^{15}) may additionally be
 10 chosen from O- C_{0-7} -alkyl, O- C_{3-6} -cycloalkyl, O-Ar- C_{0-7} -alkyl, S- C_{0-7} -alkyl, S- C_{3-6} -cycloalkyl, S-Ar- C_{0-7} -alkyl, NH- C_{0-7} -alkyl, NH- C_{3-6} -cycloalkyl, NH-Ar- C_{0-7} -alkyl, N-(C_{0-7} -alkyl)₂, N-(C_{3-6} -cycloalkyl)₂, and N-(Ar- C_{0-7} -alkyl)₂;

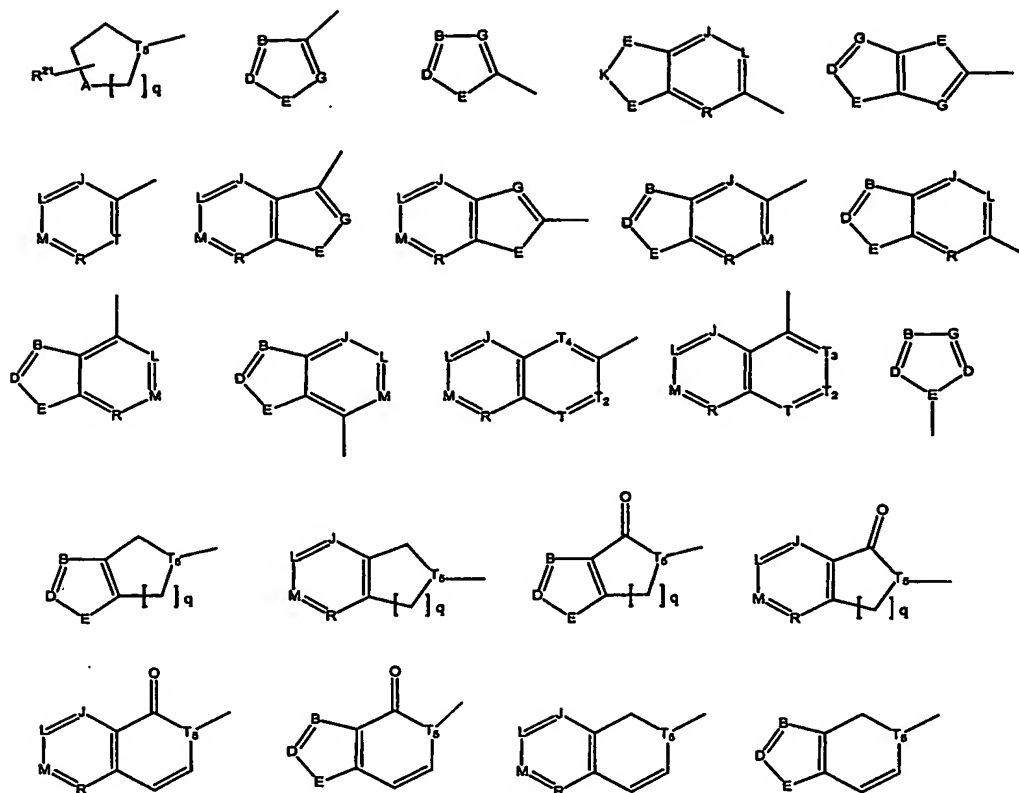
15 $(X)_0 = CR^{16}R^{17}$, where R^{16} and R^{17} are independently chosen from C_{0-7} -alkyl, C_{3-6} -cycloalkyl and Ar- C_{0-7} -alkyl and o is a number from zero to three;

$(W)_n = O, S, C(O), S(O) \text{ or } S(O)_2 \text{ or } NR^{18}$, where R^{18} is chosen from C_{0-7} -alkyl, C_{3-6} -cycloalkyl and Ar- C_{0-7} -alkyl and n is zero or one;

20 $(V)_m = C(O), C(S), S(O), S(O)_2, S(O)_2NH, OC(O), NHC(O), NHS(O), NHS(O)_2, OC(O)NH, C(O)NH \text{ or } CR^{19}R^{20}$, where R^{19} and R^{20} are independently chosen from C_{0-7} -alkyl, C_{3-6} -cycloalkyl, Ar- C_{0-7} -alkyl and m is a number from zero to three, provided that when m is greater than one, $(V)_m$ contains a maximum of one carbonyl or sulphonyl
 25 group;

U = a stable 5- to 7-membered monocyclic or a stable 8- to 11-membered bicyclic ring which is either saturated or unsaturated and which includes zero to four heteroatoms (as detailed below):

-243-



wherein R^{21} is:

C_{0-7} -alkyl, C_{3-6} -cycloalkyl, Ar- C_{0-7} -alkyl, O- C_{0-7} -alkyl, O- C_{3-6} -cycloalkyl, O-Ar- C_{0-7} -alkyl, S- C_{0-7} -alkyl, S- C_{3-6} -cycloalkyl, S-Ar- C_{0-7} -alkyl, NH- C_{0-7} -alkyl, NH- C_{3-6} -cycloalkyl, NH-Ar- C_{0-7} -alkyl, $N(C_{0-7}\text{-alkyl})_2$, $N(C_{3-6}\text{-cycloalkyl})_2$ or $N(\text{Ar-}C_{0-7}\text{-alkyl})_2$; or, when part of a CHR^{21} or CR^{21} group, R^{21} may be halogen;

A is chosen from:

CH_2 , CHR^{21} , O, S, SO_2 , NR^{22} or N-oxide ($\text{N}\rightarrow\text{O}$), where R^{21} is as defined above; and R^{22} is chosen from C_{0-7} -alkyl, C_{3-6} -cycloalkyl and Ar- C_{0-7} -alkyl;

B, D and G are independently chosen from:

-244-

CR^{21} , where R^{21} is as defined above, or N or N-oxide ($N \rightarrow O$);

E is chosen from:

5 CH_2 , CHR^{21} , O, S, SO_2 , NR^{22} or N-oxide ($N \rightarrow O$), where R^{21} and R^{22} are defined as above;

K is chosen from:

10 CH_2 , CHR^{22} , where R^{22} is defined as above;

J, L, M, R, T, T_2 , T_3 and T_4 are independently chosen from:

CR^{21} where R^{21} is as defined above, or N or N-oxide ($N \rightarrow O$);

15 T_5 is chosen from:

CH or N;

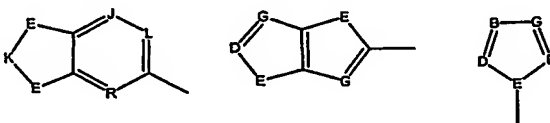
q is a number from one to three, thereby defining a 5-, 6- or 7-membered ring;

20

$R^1 = R^2C(O)$, $R^2OC(O)$, R^2SO_2 , where R^2 is chosen from C_{1-7} -alkyl, C_{3-6} -cycloalkyl or Ar- C_{0-7} -alkyl (when $C = 0$, R^1 is simply an aromatic moiety Ar);

25

provided that when Y is other than $CR^{10}R^{11}-C(O)$ or when U is:



R^1 may also be C_{0-7} -alkyl, C_{3-6} -cycloalkyl or Ar- C_{0-7} -alkyl.

-245-

5 and their salts, hydrates, solvates, complexes and prodrugs are inhibitors of cathepsin K and other cysteine protease inhibitors and are useful as therapeutic agents, for example in osteoporosis, Paget's disease gingival diseases such as gingivitis and periodontitis, hypercalcaemia of malignancy, metabolic bone disease, diseases involving matrix or cartilage degradation, in particular osteoarthritis and rheumatoid arthritis and neoplastic diseases. The compounds are also useful for validating therapeutic target compounds.

10750 132147 5177
10750 132147 5177
10750 132147 5177
10750 132147 5177